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General Charles James Fox, M.D.
HARTFORD, CONN.

TRANSACTIONS OF THE

SECTION ON

Practice of Medicine

of the
American Medical Association
at the Sixtieth Annual Session, held at Atlantic City, N. J., June 8 to 11, 1909

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MEDICAL SUPERVISION OF ATHLETICS AMONG BOYS AT BOARDING SCHOOL

NATHANIEL BOWDITCH POTTER, M.D.
NEW YORK
AND
JAMES TAYLOR HARRINGTON, M.D.
SUMMIT, N. J.

Several years ago a boy of 15 was brought to one of us with a markedly dilated heart. For some weeks he had been running a mile nearly every afternoon at one of the best-known boarding schools in New England. Since then, among others, a boy with pulmonary tuberculosis, another with so-called physiologic albuminuria, another with leukemia, a fourth with pronounced cardiac insufficiency and much overgrown, from four different and all excellent boarding schools, have been brought to the attention of one of us, and in none of them had their condition been recognized or properly studied. The observation of these cases stimulated this preliminary study of selected boys before and after exercise at a number of boarding-schools.

We first examined 38 boys, 36 of them from five boarding schools, two in Connecticut, two in New York and one in New Jersey; and 2 of the boys from a day school in New York City. After examination each boy ran a mile at his own pace, was re-examined immediately on finishing the run, and in most instances a third time, from one-half to three-quarters of an hour later. The accompanying table shows the results of our examinations.

The method followed in each case was, first, to count the pulse and to estimate the systolic blood-pressure in

the vertical posture; then to determine in the horizontal posture whether there existed any increase of cardiac dulness, the relations of the pulmonic and aortic second sounds, the presence of apical or basal murmurs and the existence of a thrill; and, while the boy was still in the recumbent posture, to count the pulse again and to estimate the systolic blood-pressure. The first specimen of urine was passed by each boy just before the run and, with the exception of the nine boys at School A, the second specimen was passed during the time of the third examination, one-half to three-quarters of an hour after the exercise. In School A a period of about two hours elapsed after the exercise before the second specimens were voided. These specimens were all examined as freshly as possible by Dr. Wilson G. Wood, to whom our thanks are due. He, of course, knew no details of our physical examination.

Selection of Boys.—At each school an effort was made to select half the number from boys especially vigorous, athletic, muscular and well developed, and the other half from boys who had grown considerably especially in height during the past two years. This effort was only partially successful.

Selection of Exercise.—It was found impossible to examine boys before and after a contest. One of us made this attempt at a dual meet between two schools but failed. The interest was centered elsewhere and the noise and confusion rendered examination impracticable. We chose a mile run as being a good test of strength and endurance for boys of this age, able to participate in football, hockey, basket-ball, track athletics, rowing and baseball. Each boy was told to take his own time and not to overexert himself, but to finish his run reasonably strong. There was no competition, although the boys were interested and some of them surprised at the time they made. Generally speaking, the most athletic of the boys made the best time and usually showed the least effect of the exertion.

We wish to call especial attention to some of the features of the examination in the following:

School A.—Nine boys training for the crew were selected. After examination each boy ran a mile at his own speed. No. 4, aged 18, one of the best oarsmen and said to be the hardest worker, exhibited a reverse blood-pressure,[1] an enlarged heart both to the right and left, a loud systolic murmur at the apex and base, an accentuated pulmonic second sound, and a slight thrill at the apex. His urine, voided after exercise, showed a marked trace of albumin, and casts were detected in both specimens. The boy stated that he tasted blood during the run, and that this was a usual occurrence with him during or after hard exercise. Two other boys exhibited casts in both specimens. Three other boys exhibited albumin in both specimens.

School B.—Nine boys were selected as well as possible according to the plan specified above. No. 17, aged 19, the best runner in the school, who recently broke the school record for a mile, ran his mile easily and in good time. He exhibited an enlarged heart both to the right and the left, a heaving apex-beat, a systolic murmur at the apex and base, and an accentuated pulmonic second sound. His urine, voided after the run, showed a marked trace of albumin.

No. 11, aged 19, a large, muscular, strong boy, was said to have injured his heart playing football two years before. He showed a reverse blood-pressure, a slight emphysema, a slight increase of cardiac dulness to the left, a systolic murmur at the apex and an accentuated pulmonic second sound. His urine, voided after exercise, exhibited a faint trace of albumin.

1. This method of testing the blood pressure was suggested to us by Dr. George L. Meylan, Adjunct Professor of Physical Education, Columbia University. The existence of what we have termed a "reverse blood-pressure," i. e. a higher blood-pressure in the horizontal than the vertical posture, he tells us, has often suggested some circulatory weakness which seems wise to supervise by repeated examination before a student is allowed to compete for a position on some college team.

No. 10, aged 17, a tall, slight boy, who had grown four inches in the past year, had been compelled during the winter to enter a lower form. He has had digestive disturbances, some circulatory weakness and several attacks of furunculosis during the past two years. He exhibited a reverse blood-pressure; his pulse before exercise was 118 in the vertical posture and 96 in the horizontal; after exercise, 152 and 124. His cardiac dulness was diminished, and he was exhausted after the exercise. Albumin and casts were found in both specimens of urine.

School C.—Eight boys were selected at random. No. 20, aged 17½, was a large, well-developed boy, had ruptured a vessel in the sclera of one eye a few days before while wrestling. He exhibited a high blood-pressure, vertical 175 mm., horizontal 150 mm., before exercise. His heart was enlarged, there was a loud systolic murmur at apex and base, and an accentuated pulmonic second sound. Both albumin and casts were present in the urine voided after the run.

School D.—Seven boys were selected from those who were training for track athletics; all of them showed albumin, and three of them casts, in the specimens of urine passed after the exercise.

No. 30, aged 15, a tall boy with remarkably well-developed legs and thighs, had grown decidedly during the past year. His pulse was 180 after the run. His blood-pressure was rather high before and rather low after the exercise. His urine contained albumin and casts in both specimens, and in the one voided after the run the albumin was a heavy trace and the casts were in great abundance.

In addition to these thirty-eight boys, six boys at School G in Massachusetts were examined before and after a quarter-mile run, the results of which are summarized in Table 2.

AGES, 15 TO 19 YEARS; AVERAGE, 17 YEARS. TIME OF RUN, 61 TO 72 SECONDS

	No.	%
Pulse		
Irregular pulse	3	50
80 or above, before	2	33⅓
Horizontal > Vertical	0	0
150 or more, after	0	0
112 or more, half hour after	0	0
Blood-Pressure		
H> V, before	3	50
H> V, half hour after	1	16⅔
150 M.m. or above, before	0	0
Heart		
Dulness + to Right	2	33⅓
Dulness + to Left	1	16⅔
Dulness + above	0	0
Pulse 2°+	2	33⅓
Aortic+	2	33⅓
Apical murmur	2	33⅓
Basal murmur	3	50
Thrill	2	33⅓
Urine		
No mkd. + indican; no acetone	.	..
Albumin, before	2	33⅓
Casts, before	0	0
Albumin, after	2	33⅓
Casts, after	1	16⅔
Red blood cells	1	16⅔

One of these boys, at the age of 13, exercised unduly the first year he passed at this school and was found to have a dilated heart when he returned home on a vacation. Our examination, made at the age of 19, showed slight thickening of the arteries, slight cyanotic color, an enlarged heart, a loud systolic murmur at the base, and an accentuated pulmonic second sound.

Eight boys were examined at School H in Massachusetts, before a one and a half mile practice row, and four of them after the row. Two exhibited a reverse blood-pressure. Albumin was found in all four specimens of urine voided after exercise; the sediments were not examined because the urine had decomposed. One of these four boys showed after the row, in addition to the reverse blood-pressure, a moderate cardiac dilatation and slight evidence of exhaustion.

Six of the Columbia freshman crew, ages 16 to 22, average 18½, were examined before and after a light practice row. The blood-pressure was reversed in three

50 per cent. One of these three, who had been under Dr. Meylan's observation on account of a rapid pulse persisting after an attack of influenza in February, showed in the examination of urine after the row a heavy cloud of albumin and many casts. Another, aged 19, had grown markedly in the past year. The examination of the urine, both before and after, showed a trace of albumin and many casts in the specimen after the exercise. Another of these, aged 18, was the only one who showed any evidence of fatigue after the light row. He exhibited some emphysema. He had played water polo hard during the winter. There was a cloud of albumin and casts in the specimen taken after the exercise.

Ten Marathon runners were examined after the race, and all except one exhibited a low blood-pressure; 90 to 100 mm. The exception, the winner, showed 160 after and 120 before. Three were examined before and after another race. In the examination afterward all showed a blood-pressure below 105, while in that made before all showed a blood-pressure above 140.

These examinations show that some of the boys should not be allowed to take part in strenuous exercises or competitive sports unless carefully supervised by a competent physician. Permanent physical injury has resulted in the past which might have been prevented by careful watching; and the same harm will occur in the future. In most of the schools we visited an earnest effort has already been made to watch the boys more carefully; but, in our judgment, it was more in the direction of copying the college athletic training, in the effort to turn out winners, than with the idea of individualization and careful medical supervision. Even a competent supervisor is hardly capable of discriminating in some of the border-line cases cited above as to whether to permit exercise, to increase or to diminish it. The school physician examines each boy in the fall and again whenever called on to do so; but we found no defi-

nite, purposeful method of physical or urinary examination before or after such a functional test as we applied; nor any plan for an examination by the school physician before and after hard-matched games, although the frequency of the latter in some of the schools was quite as striking as at colleges. One of these physicians told us that some of the boys grew so rapidly that the fall examination was of little or no value in the spring.

It is not the province of this paper to discuss the significance of albumin and casts in the urinary analysis before and after exercise. Darling and others have shown that albumin and casts appear very often in the urine of young healthy adults after severe exercise. But some of our specimens showed albumin and casts before exercise and others showed a considerable amount of albumin and a great many casts after exercise. Such cases are evidently on the border-line between health and disease, if not beyond it, and merit careful supervision and individualization. Nor do we propose to dilate on the type of physical examination or functional test. A mile run is obviously too severe a strain for some boys, but, if so, these boys should not be allowed to compete in hard contests. From the results of the tests we made it is evident that many of the boys require as much careful supervision over their athletics as they do over their lessons.

It is an important question to determine the advisability of so much devotion to athletics among school boys; but it is within the range of this paper only to urge proper medical supervision over a part of the schoolboy's life, which in his eyes at least is quite as important as his studies. Colleges foster the spirit of competitive games; newspapers dilate on them; the age demands athletic development in the youth; but a growing boy, crowded hard at his lessons so as to pass his college examinations, may not be able to withstand repeated and continued athletic training.

48 West Fifty-first Street.

DR. DE LANCEY ROCHESTER, Buffalo, N. Y.: I was much interested in Dr. Potter's paper, because of the occurrence of three cases of serious heart trouble which developed in boys under my observation who were engaged in school athletics. A point not brought out in the paper was the evil occasionally resulting from jumping. I have seen one case of flatfoot from this. I think one of the most serious things in athletic contests is the fact that they are contests. Games in schools are very good for the children; but I think that competition, which enters so largely into these contests, makes the boys overdo it to a great extent. Moreover, athletics are now appearing in the lower grades of schools, and I have now under observation two boys, 8 years of age, who have been injured by these athletic contests in school. These children are encouraged by their masters, and I believe there is great danger of the masters encouraging the boys too much, urging them on in these athletic contests to the physical injury of the boys.

DR. RICHARD C. CABOT, Boston: Dr. Potter's paper backs up the conclusions reached by Dr. Darling of Cambridge in his observations on certain athletes, such as football players, An interesting point which Dr. Darling emphasized is that in fatigue we get conditions, not exactly healthy or exactly diseased, according to ordinary conceptions. He found in fatigue states not only a marked leucocytosis, but abnormal forms of leucocytes, such as are not to be discovered at all in health. Yet all these things apparently work no permanent harm to the individual. In one of Dr. Darling's cases (after a boat race) anyone would have said that the urine showed an acute nephritis; there was present a large amount of albumin, blood and many casts. Yet within a few days the urine was normal again. To me an interesting point is that from mere fatigue such changes can be produced in the heart, the blood and the kidneys. I should like to ask Dr. Potter the reason for this "reversed blood pressure." Why was it greater in the horizontal than in the upright position?

DR. STANLEY P. BLACK, Pasadena, Cal.: I should like to know how many of these athletes develop endocarditis, a severe endocarditis. I am afraid that we are developing heart troubles in the children. A child of 8 years is now taught to run one mile. I have seen young children run until they fall from exhaustion, unconscious on the track. I think it is an outrage that such is allowed, and the medical profession should enter a protest against the manner athletics is often carried on in schools to-day.

DR. NATHANIEL BOWDITCH POTTER, New York: We attempted to estimate the blood pressure in the horizontal and in the upright position, because Dr. Meylan, in examining students at Columbia University, found that students whose vertical pressure was lower than the horizontal pressure needed careful

watching. In our observations we hoped to find something definite from the test, but I can not say that we did. Many of the boys showed rather excessive fatigue after the race, presented a greater amount of albumin and a larger number of casts, or showed an abnormal heart's action, and some of these boys exhibited a reverse pressure which most of the others did not. In one of the schools where I examined six boys before and after a quarter-mile run, one boy exhibited a marked cardiac enlargement and a reverse blood pressure. Six years before, while at home on his vacation, Dr. Favill of Chicago asked Dr. Billings to examine the boy's heart. The boy had a dilated heart.

THE USES AND LIMITATIONS OF EXAMINATIONS OF THE STOMACH CONTENTS

CHARLES G. STOCKTON, M.D.
BUFFALO, N. Y.

The stomach-tube should not be too small; for an adult it should be from 30 to 35 French scale. It should not be too flexible; it should suport its own weight held in the upright position for the length of twelve inches without bending. It should have the largest caliber possible without making it liable to bend sharply at an angle when pressed on. A good deal depends on the quality of the rubber; much depends on the character of the tube. It should have no pumping apparatus connected with it and it should be about 54 inches long.

On the introduction of the tube it is occasionally grasped by the esophagus about 8 or 10 inches from the teeth. If this delay is temporary, it depends on spasm, and one may expect to find either cardiospasmus or stricture at the cardia.

Finding portions of the test meal returned when the tube has passed about 14 inches, the food being unmixed with gastric juice, is evidence of obstruction of some kind at the cardia, the retention of food in the esophagus and probably dilatation of the latter.

If in pressing the tube onward it stops at the cardia or, engaging in a spasmodic contraction, is held fast, we may infer the existence of stricture or spasm at the end of the esophagus.

On passing the tube into the stomach we usually obtain the best reflow at a distance of from 21 to 22 inches

from the teeth, provided the patient is an adult of ordinary stature, having the stomach in position and of normal size.

Where the stomach is high this result may be obtained at 18 inches. In a very tall person the tube may have to be passed 24 inches or beyond, even when the stomach is in a normal position.

When the tube is passed 20 to 22 inches we may find stomach contents; and on aspirating this, the tube being pressed further on, after a little resistance, it apparently gets into a second cavity from which stomach contents of different character is removed. This indicates an hour-glass stomach or a spasmodic contraction of the stomach between the second and the last third of the organ; in other words, at the antrum pylori.

When, after passing the tube the usual distance, we find present an unusually large amount of the test meal at the proper time, it indicates moderate motor insufficiency of the stomach which may depend on atony or on some opposition at the pylorus.

If we find a large quantity of the test meal present undergoing fermentation, having a "musty" odor, showing a large quantity of bacteria and sarcinæ and full secretion of hydrochloric acid, with few lactic acid bacilli, it is indicative of benign obstruction at the pylorus.

If we find stagnating food of foul odor, either with or without free hydrochloric acid, with lactic acid present, together with the Oppler-Boas bacilli and unchanged or occult blood, it suggests malignancy and obstruction.

The presence of too little of the test meal at the usual time with, however, the presence of gastric juice, suggests overmotor activity.

When we find the stomach empty or find present too little of the test meal and no gastric juice, it indicates an excessive motor activity, probably associated with achylia gastrica (a condition frequently present in pernicious anemia).

A conclusion should not be reached by a single examination. On one day there may be found the absence of gastric secretion and on the next an excess of it. On one day the food may be retained beyond the usual time and on another it may have passed onward too quickly. From this we conclude that the patient is the subject of nervous disturbance, perhaps excited by the very practice of lavage.

When we find habitually an acidity above 60, depending on hydrochloric acid, free or combined, the presence of hyperchlorhydria is suggested.

Hyperchlorhydria, however, is not to be determined by a given standard. The secretions of the stomach are seldom stable and should not be fixed by positive laws. A secretion normal with one person is excessive with another. In other words, some patients suffer from the symptoms of hyperchlorhydria when the secretion is decidedly below the standard. Such patients may be victims of gastric hyperesthesia.

There are cases of practical suspension of the gastric secretory function with symptoms similar to those of hyperchlorhydria; these are probably instances of chronic glandular gastritis with exacerbations accompanied by symptoms of irritation.

Overacidity, with delay in digestion of starch, is indicative of hyperchlorhydria.

A high total acidity, depending mostly on free hydrochloric acid, suggests a defect in secretion of enzymes.

A high total acidity, depending largely on combined chlorids, suggests an active secretion of the enzymes.

The presence of mucus in excess should always attract attention. Large quantities of glairy, ropy mucus, unmixed with the test meal, indicates esophageal mucus which has entered the stomach through the irritation ocasioned by the passing of the tube. It often occurs when the tube has been introduced in a clumsy manner. It is not indicative of gastritis.

Finding a mass of nummular sputa, often accompanied by pus and by epithelium from the respiratory tract, indicates that the mucus has been swallowed and is not of stomach origin.

When mucus is found thoroughly intermixed with the test meal, usually not glairy or ropy, it probably comes from the gastric mucosa, and is indicative of catarrhal gastritis.

The presence of occult blood, or blood cells having undergone change by digestion, is evidence that hemorrhage has taken place in the stomach with active secretion such as occurs in ulcer.

If the blood cels are found intact it speaks for recent hemorrhage or lack of digestive power, or both.

The presence of blood with mucus and pus cells, apparently not coming from the respiratory passages, with fragments of tissue, suggests ulceration or degeneration of the gastric mucosa and probably malignancy.

A slow return of the gastric contents through the tube, showing little pressure from below, is indicative of atony and probably of dilatation.

Finding food remaining after washing for a considerable time is evidence of atony and probably dilatation.

Finding that the stomach holds, without inconvenience, a large quantity of fluid is indicative of dilatation; however, testing the capacity of the organ in this manner is a practice not recommended.

On the other hand, if the stomach contents return through the tube with some force, it indicates a strong motor activity or a stomach greatly overdistended with contents—certainly a high pressure. (Under such circumstances we should attempt to rule out the elements of strong contraction of the abdominal muscles.)

A forcible return may occur in dilatation provided there is hypertrophy of the muscle walls as a result of pyloric stenosis.

Violent or spasmodic spurts, coming from the stomach-tube, result from sudden contraction of the abdominal muscles and a suddenly increased intra-abdomintl pressure.

When bile is found in the stomach contents it probably depends on relaxation of the pylorus with upward pressure of the duodenal contents through contraction of the abdominal muscles, or reverse peristalsis.

When the proximal end of the tube is held beneath water and bubbles of gas escape through it, it is indicative of an excess of gas in the stomach.

When no gas escapes from the stomach, even though the patient complains of continuous eructations, it may be argued that the gas is not formed in the stomach by fermentation, but that we are dealing with a hysterical condition.

The slow change of albumin, especially of meat fibers, shows that the gastric digestion is retarded.

The presence of the odor of fatty acids, of a "musty" or vinous odor, is evidence of fermentation.

Too much importance should not be attributed in stomach examinations to the disturbances in secretion.

The greatest importance should be attributed to evidence of disturbances in motion.

The diagnosis of stomach diseases should not be made solely by examination of the gastric contents, but by the results of this method considered in connection with the symptomatology and with the estimation of all the facts in the case.

Wrong conceptions will arise from basing a diagnosis on stomach examinations alone, or on too infrequent examinations; or on examinations conducted without rules and without thought.

The stomach-tube is of the greatest importance in the matter of diagnosis; in treatment it is often useless and sometimes pernicious. Nevertheless it is at times a therapeutic agent of great efficiency and cannot be replaced

by any other measure in poisoning cases, gastrectasis, before operation in obstruction, in some cases of intractable vomiting, in catarrhal gastritis and, in general, for the relief of an irritable gastric mucosa.'

It should be much more generally employed than it is as a routine in general examinations, but, as in other physical methods of examination, the results will depend on the expertness and thoughtfulness of the examiner.

436 Franklin Street.

X-RAY EVIDENCE IN GASTRIC CANCER

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The treatment of cancer of the stomach rests in the hands of the surgeon, but the diagnosis rests in the brain of the physician. He is the first to see the case. If he fails to make an early diagnosis the surgeon can give no hope. And yet early diagnosis is often impossible even with the advantages of experience and the laboratory. For these reasons I hope to interest the internists of this Section in a comparatively new factor in the early diagnosis of cancer of the stomach. This factor is the *x*-ray plate.

The use of the *x*-ray in diseases of the alimentary tube depends on the fact that the inside of the stomach or intestine, when coated with a salt of bismuth, casts its shadow on plate or screen. In such shadows lie the *x*-ray evidence of gastric disease. These skiagraphs are not self-interpreting. A known and constant technic is a condition precedent. In addition to an *x*-ray training we must bring to bear the physical examination of the case, the laboratory findings, the inspection through the incision at operation, and the investigations of the post-mortem. The larger the record of a collective experience of many workers the more exact and comprehensive will be the interpretation of skiagraphs.

This illustrates the fact that we are in the primitive stage of the *x*-ray diagnosis of gastric cancer, and justifies me in assembling the diagnostic factors deducible from the *x*-ray image of the inner wall of the stomach, so as to consider those attributable to cancer.

The diagnostic factors presented are:

1. Size.
2. Form.
3. Position.
4. Clearance.
5. Location of pain-marker.

The size of the stomach must be judged by the size of the patient. The form of the stomach, which is subject to change without notice, may nevertheless clearly be designated as:

1. Normal stomach.
2. Tubular stomach.
3. Globular stomach.
4. Drain-trap stomach.
5. Deformed stomach.
    a. Indentation stomach.
        (1) From spleen or other adjacent organ.
        (2) From tumor in stomach wall.
        (3) From tumor outside stomach.
    b. Adherent stomach.
    c. Contractured stomach.
        (1) Forming pucker in body of stomach.
        (2) Forming hour-glass contraction.
        (3) Forming partial or complete stenosis at pylorus.

The position of the stomach may be normal, or may be displaced as a whole, or may suffer a displacement of certain parts, namely, the fundus, the greater curvature and the pylorus with its antrum.

If the center of pain, or of tenderness on pressure, be marked by a lead letter (P) fastened to the skin by adhesive plaster, we may find the demonstration of this displacement of the stomach or its parts, with reference to the lead letter as depicted on the *x*-ray plate, to be a matter of decisive importance. The stomach or its parts may extend to unexpected places. The lead marker, which we thought lay over the appendix, we may find to coincide with the pylorus; or, again, the lead marker,

which we thought lay over the stomach, may lie over the pancreatic area, the stomach having prolapsed out of the way. Incidental to a stomach examination we may demonstrate the lead marker of pain or tenderness to coincide with the duodenum or some other portion of the small intestines, some part of the colon, or the spleen, liver, gall bladder, kidney, ureter or urinary bladder. But the position of the lead marker must not be implicitly relied on to localize the lesion. For example, a circumscribed abdominal pain may be due to a Pott's disease of the spine high up in the dorsal vertebræ, beyond the field of the stomach plate.

Our fourth factor, the clearance of the stomach or its power to empty its contents, depends on:

1. Position of greater curvature.
2. Position of pylorus.
3. Pyloric stenosis.
4. Pyloric insufficiency.
5. Hour-glass constriction.

An analysis of these diagnostic factors presented by stomach skiagraph shows that three out of five major factors may give information concerning gastric cancer. They are:

1. Form.
2. Location of lead marker.
3. Stomach clearance.

In the case of cancer the alterations of form are those of the indentation or contractured type of the deformed stomach. In the case of ulcer the alteration is confined to the contractured type. The indentation stomach is therefore the type distinctive of cancer. A benign growth would have to be excluded on other grounds.

The factor of stomach clearance is observed in the last plate. If bismuth remains an unusual time in the stomach, there may be a pyloric narrowing or an hour-glass contraction due to the scars of old sores or to indentations. Lastly, if the lead marker lies over a

certain portion of the stomach and the case history shows the location of pain or tenderness to be constant, then we may add this fact to the other clinical data favoring cancer. By the same reasoning, if the marker lies over the duodenum we may suspect duodenal ulcer.

But the *x*-ray diagnostician must never judge a case from *x*-ray signs alone. He must possess himself of the entire clinical and laboratory records. The *x*-ray amplifies but does not supersede other means of diagnosis, although it often happens that the skiagraph supplies the missing premise of a diagnostic syllogism.

The problem of differential diagnosis may require a careful consideration of all available evidence in the case. When we find a deformed gastric outline we have to discriminate between an indentation from the pressure of other organs or growths; a local contraction of the stomach wall; an invasion of the stomach wall by a growth; and the presence of adhesions due to disease of contiguous organs. Also when we find low clearance and a globular form, and establish the fact of pyloric narrowing, we then have to discriminate between narrowing due to the scar tissue of ulcer; that due to growths in the walls of the antrum or pylorus; that due to pressure of growths or glands outside of the pylorus; and that due to binding of adhesions.

In order to make these discriminations we must study the stomach under normal conditions so as to be able to recognize a departure from normal outlines. The normal stomach is more vertical than horizontal and lies above the plane of the umbilicus. Laterally, the axis of the stomach is oblique to that of the trunk, the fundus lying to the back and the pylorus to the front, so that when the patient is placed horizontally on his back the stomach contents gravitate to the fundus and, when placed on his abdomen, to the pylorus. The fundus is in contact with the diaphragm above, the left lobe of the liver to the right, and the spleen to the left and

back. The main body of the stomach lies posteriorly in contact with the tail of the pancreas, the left kidney and suprarenal. On the left side it lies in contact with the spleen, the splenic flexure of the colon, the transverse colon, and the descending colon. On the right it lies against the vertebral column and the abdominal vessels. The antrum pylori at the back lies against the pancreas, while the whole stomach in front lies against the abdominal wall. The displaced or dilated stomach may lie in contact with any and every organ in the abdominal cavity.

When we consider the contact relations of the stomach we see that a study of the indentations of the stomach walls may in different cases yield information concerning almost every abdominal organ.

Our technic must be adapted to these anatomical conditions. Air or bismuth within the stomach gives certain outlines. In actual practice by the bismuth method we have to do with the combination, since air or gas is always present to some extent. We must consider the following points:

Patient.

1. Position of body.
2. Degree of stomach distension.
3. Contents of stomach.
4. Immobility.

Bismuth.

1. Kind of salt.
2. Quality.
3. How suspended.
4. How taken.
5. How distributed.

Time of day for exposure of plates.

1. Relation to meals.
2. Time elapsing between ingestion of bismuth and exposure of plate.
3. Number of plates and time between.

The patient may be in any position, but the best skiagraphs will be obtained by placing the patient horizontally, front down, on the plate.

Only by the horizontal position can we prevent the bismuth by its weight from deforming the true gastric outline. The preservation of the true gastric outline also depends on the degree of stomach distension and the nature of the stomach contents. The stomach should be empty to begin with and the distribution of bismuth should be such as to reveal most surely any indentations, contractures, or adhesions. This part of the technic must be an approximation because we can only approximate the size of the stomach preceding our *x*-ray plate.

Immobility of the patient may be obtained by having the breath held. Practical immobility of the stomach may be obtained by sufficiently rapid exposure, or by morphin. Morphin, however, destroys to a large extent the value of the second and third plates by interfering with the factor of stomach clearance and the intestinal distribution of the bismuth.

Nearly all of my stomach work since 1905, until two months ago, has been done with bismuth subnitrate. With the exposure of the final plate I have always given a full dose of Epsom salts. An average of three cases in a hundred, however, have shown some slight toxic symptoms consisting of faintness, cyanosis, slight pains and stiffness of the legs from ten to twenty-four hours after. With the Epsom salts following, I believe that bismuth subnitrate may be safely used. The subcarbonate, however, first suggested to me by Dr. Pfahler, gives equally good skiagraphs, and is free from the possibility of the decomposition of the nitrate radicle with the formation of poisonous nitrites.

The method of mixing the bismuth with some kind of foodstuff so as to fill the stomach does not meet our diagnostic requirements. The aim is not to fill the stomach, but to coat its walls; not to show a large bolus of food and bismuth, but to define stomach outlines.

To this end the bismuth should be introduced into the stomach in the thinnest menstruum that can be swallowed. This is plain water.

The quantity of bismuth needed is, according to the size of the patient, from 40 to 100 gms. in from 250 to 500 c.c. of water. This is immediately distributed over the rough and furrowed mucosa of the stomach by placing the patient in the horizontal position, back down, on a swivel surgical chair or table, which is then tipped into the Trendelenburg position, head lowered, feet up. We may then slowly rotate the chair while the bismuth is settling upon the stomach lining, where it will be retained for a time which is more than ample for skiagraphic purposes. The patient is then directed to turn over via the left side, face down, without rising out of the horizontal, after which the chair is again tipped, head down, and rotated as before. From three to five minutes are sufficient for these maneuvers. The patient, now in the horizontal position, face down, arches the abdomen to allow a plate to be placed beneath. He then lies on the plate, care being taken to bring the arms forward so that the weight of the body is not supported by the elbows. A 14 by 17 plate should be placed so that the forward edge is on a line with the nipples. The tube should then be fixed, not closer than 50 cm. (or about 20 inches), over the center of the plate. The radial axis is then always in the center of the plate and need not be marked by plumb, as in my earlier plates.

If the preparations have been complete, including the previous fixing of a lead U in the umbilicus and a lead P over the center of the area of pain or tenderness, if such exist, then we shall be ready to turn on the *x*-ray in from five to fifteen minutes after giving the bismuth. The patient is directed to take a moderate breath and hold it as long as he can without moving in any way. This allows us from five to thirty seconds, according to the size of the patient, and ensures a serviceable nega-

tive in every case. The shorter the time the clearer-cut th negative. But all the time up to thirty seconds may be allowed which the apparatus requires.

The first plate (14 by 17) may be conveniently exposed in the morning after the test breakfast has been withdrawn for analysis. Then, an hour after the first plate, a second plate (10 by 12 or 8 by 10) should be exposed under a compression diaphragm so as to take in any area which the first plate shows as abnormal. If no such abnormality appears, then one should focus over the critical area within which lie the antrum pylori, the pylorus, the duodenum, the head of the pancreas and the common duct. Six hours after the first plate, or the time between two meals, a third plate (14 by 17) should be exposed. This will demonstrate stomach clearance, confirm gastric deformities, and show the intestinal distribution of the bismuth. If the first plate is exposed before dinner the third may be exposed before supper. After the first plate the meals should be eaten as usual.

As to the technic of coil, tube and plate, I would say only that skiagraphy of the alimentary tract by the bismuth method is hard-tissue skiagraphy, the bismuth areas often greatly exceeding the bones in density, as shown by stomach negatives.

The progress of the bismuth is often astonishingly rapid. In five minutes after the bismuth is taken a portion of the duodenum will commonly be coated. In fifteen minutes bismuth may be found in the jejunum, and not infrequently in coils of the ileum. In four hours the stomach may have emptied itself; and in four to six hours, the small intestines, by their vigorous peristalsis, may have passed the bismuth clearly and completely into the colon, where it may be distributed from the cecum to the sigmoid.

These points and each essential condition and factor mentioned in this paper are illustrated by seventy-two plates placed in observation frames in the Scientific

Exhibit. Lack of time prevents me from demonstrating them on this platform. These are the best of several hundred plates taken by myself in the course of a private and consultation practice, and have been carefully labeled and described by typewritten sheets posted on the frames. I have been aided in the interpretation of each plate by my relation of physician to the patient, by a necessary familiarity with the clinical and laboratory findings, and by attendance on most of the cases for subsequent periods. When operation or autopsy has followed, such is indicated on the plate. This exhibit is arranged particularly for medical men who are not *x*-ray experts, because so many medical men, even some of national fame, seem strangely unaware of the possibilities of the *x*-ray plate.

I believe that sufficient stomach work has already been done by numerous *x*-ray operators in various parts of the world to demonstrate the incomparable value of the *x*-ray in cancer of the stomach as well as in a wide range of other affections of the alimentary tube. Medical men should study *x*-ray plates of their cases. It is no exaggeration to say that the *x*-ray plate and screen will give often more and better information than an exploratory operation. This is emphatically true in the case of gastric ulcer, but holds true in the main for gastric carcinoma. Where the diagnosis of malignant disease is not in doubt the *x*-ray should still be used, because few medical or surgical diagnoses are so exact and comprehensive that the skiagraph and screen may not extend or revise our knowledge.

In conclusion, I take pleasure in acknowledging my indebtedness to Dr. C. M. Spencer, my clinical assistant, for his very able service in this work.

420 South Rose Street.

THE DETERMINATION OF TRYPSIN IN THE STOMACH CONTENTS AFTER OIL TEST MEALS *

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The experiments reported in the following paper are based on the work of Boldireff and Volhard. The former in experiments on dogs found that the introduction of oil into the stomach caused regurgitation of duodenal contents, in which the presence of pancreatic ferments could be demonstrated; the latter devised a new method for demonstrating the presence of trypsin and applied Boldireff's discovery to clinical uses.

A. OBJECTS, METHOD AND RESULTS IN GIVING OIL TEST MEALS

My first object was to substantiate the observations of others as to the ease and frequency with which duodenal contents might be obtained after the oil meal.

The second was to decide which of the methods proposed was best suited for detecting trypsin in the specimens secured.

The third was to discover what, if any, clinical value was to be attached to the findings thus obtained.

The oil meal as given, consisted of 100 to 200 c.c. of olive-oil or cottonseed-oil; in most cases this was given through a tube; occasionally the patients preferred to drink the oil. While the tube was in the stomach, before the oil was administered, any contents present were aspirated or washed out. In the case of a large dog, in

* From the William Pepper Laboratory of Clinical Medicine.

which repeated attempts to obtain duodenal contents had failed, lavage with sodium bicarbonate solution, as well as the administration of magnesia, was tried without effect. In one-half to one hour, the oil was aspirated. In many cases a few cubic centimeters of whitish mucoid fluid, in addition to a small amount of oil, was all that could be recovered. In other cases a large amount of pale green or dark curdy green fluid, amounting in one case to as much as 250 c.c., was obtained. With this was a supernatant layer of unchanged oil and an intervening zone of soap-like emulsion. The tests were carried out in the separated white or green fluid without previous filtration.

The following is a summary of the oil test meals:

18 oil test meals were obtained from patients.
5 oil test meals were obtained from a large dog.
1 specimen was aspirated from the duodenum of a dog by intubation.
Twenty-four specimens in all were examined.
6 of these were of a light or dark green color.
18 were transparent, milky or in a very few cases brownish.
3 of the green specimens showed the presence of trypsin.
3 of the green specimens showed the absence of trypsin.
4 of the colorless specimens showed the presence of trypsin.
14 of the colorless specimens showed the absence of trypsin.

In addition four Ewald test meals, mostly green in color, were examined; one showed the presence of trypsin.

In practically all cases more or less fluid was obtained; frequently this was nothing more than a small amount of retained or possibly newly secreted gastric juice and mucus. It seemed to me, therefore, that the only criterion as to the character of the juice should be its color, indicating or not indicating the presence of bile, and its response to tests for ferments. A third factor might be the amount obtained. Judged by this standard, only nine out of the above eighteen tests on human beings can be considered successful. This differs widely from the results of a recent writer who was

successful in 48 out of 50 cases. This disparity may be accounted for partly by my lack of experience, but more largely, as I shall point out, by his faulty controls. My conclusion, therefore, is that Boldireff's plan is superior to those previously suggested, but is by no means uniformly successful as several writers have intimated.

B. COMPARATIVE VALUE OF METTE, VOLHARD AND GROSS METHODS OF TESTING FOR TRYPSIN

Of the numerous methods proposed at various times for the estimation of pepsin and trypsin only two or three, which have been used for the purpose under consideration, will be considered. Most of the others are too complicated for clinical use, or else offer no advantages over those here discussed. The Mette method, as I have described it in several previous articles, was employed and needs no minute description, as it is now fully given in the text-books. In using it for trypsin the contents were usually diluted with decinormal sodium carbonate solution, thus affording the most favorable conditions for tryptic digestion. Particles of fibrin were placed in each dish to detect traces of digestion.

The detailed technic of the Volhard method may be omitted, but it is necessary to give an outline to explain the principle on which it is based. A strong casein solution of a definite strength and alkalinity is prepared. To a measured portion of this alkaline fluid a definite amount of neutralized duodenal juice is added, and digestion allowed to proceed at 37 C. for twenty-four hours or other fixed period; then a definite but excessive amount of normal hydrochloric acid is added and the precipitation of the casein brought about by sodium sulphate. The amount of precipitate is found to be in inverse ratio to the amount of ferment, and on filtration the acidity of the filtrate, as tested by titration with decinormal sodium hydrate solution, is found to be increased directly in proportion to the amount of ferment. A control is used in each case, the acidity of the

control being substracted from that of the specimen under examination. The exact directions for the preparation of the solution are appended.

The method of Gross, which is very similar to the one simultaneously devised by Fuld, also utilizes casein as the substratum for digestion. A solution of casein, 0.1 per cent., in 0.1 per cent. sodium carbonate solution is prepared and 10 c.c. decanted into each of several test-tubes. The trypsin solution serially diluted is added and the tubes incubated for twenty-four hours. At the end of that time 1 per cent. acetic acid solution is added to each of the tubes and the dilution noted in which cloudiness is still produced. If the casein is completely digested no cloud appears.

The tests were employed first with artificial trypsin or pancreatin solutions and, secondly, with the contents obtained by Boldireff's method. Previous work with the Mette method had convinced me that it was a good, though not delicate, qualitative test of artificial trypsin solutions. In testing duodenal contents, however, I was unable to obtain any positive results. Particles of fibrin were frequently added to the dishes and almost invariably showed digestion in cases in which Volhard was positive. By the Volhard method eighteen specimens obtained from patients or from dogs after the oil meals, as well as several specimens of feces and ordinary stomach contents, were tested. Numerous experiments were also made with artificial solutions. In almost all cases the minutest traces of trypsin were clearly indicated. In a number of instances in testing duodenal contents a marked disparity was noted between a water control as used by Volhard and others, and a control consisting of the boiled specimen to be tested. These differences, as shown in the accompanying tables, were sufficient to counter-balance the low figures obtained in many of the positive results reported by others. I was also unable to obtain any definite quantitative results; occasionally the titration showed acidities closely corresponding in rela-

tive amount to the comparative strength of the trypsin solutions employed, but in the majority of instances in which trypsin solutions of varying strength were simultaneously tested, the stronger solutions gave higher results, but the figures bore no definite relation to the concentration of the ferment. In some cases this correspondence in results may have been due to the fact that the weaker solution gave a maximum effect. My conclusion was that the Volhard test had little value as a quantitative method, but was a delicate and reliable qualitative method.

The Gross test seemed to be a delicate one, but, as its inventor states, it is not suited without modification for use in duodenal contents, as bile salts and other constituents give rise to a similar precipitate which is liable to cause confusion.

My inclination in the future would be to use the Mette method and a simplified Volhard test in a purely qualitative way to control each other. I would use mensuration in the former and titration in the latter only when the results were doubtful.

The accompanying examples (Tables 1, 2 and 3) from my note-book have been arranged in tabular form to illustrate (1) the details of the dilutions and calculations, as well as (2) the results obtained by different methods and by the use of natural and artificial trypsin solutions.

Let us now pass to the clinical side of the question. My cases are too few in number to be of much value, so that after a brief outline of my results, I shall review the valuable or suggestive findings of others. As stated above, I have excluded from consideration all cases in which neither bile nor trypsin was present. This unfortunately limits the usefulness of the test, but seems to be unavoidable.

In four cases some affection of the pancreas was present or suspected.

TABLE 1.—OIL TEST MEALS FROM PATIENTS*

Titrations made with decinormal sodium hydroxid solution. Phenolphthalein used as indicator. Results corrected for acidity of specimens. Temperature of thermostat 37 C.

	1	2	3	4	
1 (p. 82†). Gastrointestinal neurosis.	Control, Water 10 c.c.	Control, 10 c.c. of boiled specimen.	"Juice" 10 c.c.	"Juice" 5 c.c. Water 5 c.c.	Remarks.
Titration	11.2	14.4	16.0	14.4	Green color.
Less 2	....	....	14.4	14.4	Time 18 hours.
Increase in acidity.			1.6	0.0	Pepsin normal and trypsin absent by Mette.
2 (p. 92). Intestinal indigestion.	Same.	Same.	Same.	Same.	Remarks.
Titration	22.6	19.4	20.4	19.7	Green color.
Less 2	....	....	19.4	19.4	Time 24? hours.
Increase in acidity.			1.0	0.3	Pepsin present and trypsin absent by fibrin test.
3 (p. 64). Cancer of pancreas.	Same.	Omitted.	Same.	Same.	Remarks.
Titration	11.2	....	20.6	20.4	Green color.
Less 1	....	....	11.2	11.2	Time 16 hours.
Increase in acidity.			9.4	9.2	Control faulty.
4 (p. 72). Gastric ulcer.	Same.	Same as 1.	Same.	Same.	Remarks.
Titration	8.8	15.2	32.0	32.4	Green color.
Less 2	....	....	15.2	15.2	Time 8 hours.
Increase in acidity.			16.8	17.2	Pepsin normal and trypsin doubtful by Mette.
5 (p. 88). Cancer of stomach.	Same.	Same.	Same.	Same.	Remarks.
Titration	13.8	20.0	52.8	51.8	Green color.
Less 2	....	....	20.0	20.0	Time 24? hours.
Increase in acidity.			32.8	31.8	Temperature of incubator irregular. Pepsin and trypsin absent by Mette test.

* This table shows a few typical cases. Nos. 1 and 2 may be regarded as negative, No. 3 shows a small amount of trypsin, Nos. 4 and 5 larger amounts. Water is shown not to be a sufficient control.

† The page numbers refer to laboratory note-book.

TABLE 2.—COMPARATIVE TESTS BY THREE METHODS, USING COMMERCIAL PANCREATIN (WYETH'S) AS DIGESTANT

Solution and dilutions made with 0.1 per cent. sodium carbonate solution.

	1	2	3	4	5	6
	Sod. carb.	Pancreatin.	Same	Same	Same	Same
VOLHARD. 10 c.c. in each.	0.1%	1.0%	0.5%	0.1%	0.05%	0.01%
Titration	18.0	71.2	72.0	63.0	57.0	28.6
Less 1		18.0	18.0	18.0	18.0	18.0
Decrease in acidity.		53.2	54.0	45.0	39.0	10.6
GROSS. 1 c.c. in 10 c.c. of casein solution.						
After addition of 1% acetic.	Milky cloud.	No cloud.	No cloud.	No cloud.	No cloud.	Faint cloud; in 0.005 % distinct cloud.
METTE and fibrin. 5 c.c.						
METTE tubes fibrin flakes.	Trace	Trace	Faint Trace	Faint Trace	Neg.	Neg.
	Dissolved.	Dissolved.	Partially? dissolved.	Neg.	Neg.	Neg.

TABLE 3.—MERCK'S TRYPSIN 1 PER CENT TESTED BY VOLHARD'S METHOD*

	10 c.c. Water.	10 c.c. Solution.	10 c.c. Solution.	5 c.c. S. 5 c.c. W.
Titration	17.6	63.2	66.4	68.0
Less 1	....	17.6	17.6	17.6
Decrease in acid.....	....	46.6	48.8	50.4

Time 3 hours.

* Many similar tests were made which agreed substantially with those given above.

CASE 1.—In the first patient, the diagnosis of cancer of the pancreas was made at operation. Previous to operation 50 c.c. of green fluid had been obtained after an oil test meal. Volhard's test gave an increase in acidity of 9.4. Unfortunately water only was used as a control. Trypsin was probably diminished in amount or possibly absent.

CASE 2.—The second case was one of cancer of the prostate with secondary growths. After an oil test meal, 3 c.c. of white fluid were obtained. The fibrin test for trypsin was positive; the Mette test was negative. At autopsy a secondary growth was found in the pancreas with necrosis of the tail of that organ and subdiaphragmatic abscess.

CASE 3.—The third case presented indefinite intestinal symptoms which were said to have been relieved by pancreatin.

The case was considered to be a gastrointestinal neurosis. Two oil test meals were examined, one specimen was white and gave a low positive result by Volhard (7.0); the other was green and contained no trypsin. The latter result seemed to be the more trustworthy.

CASE 4.—The fourth case was referred to Dr. Edsall as a probable case of pancreatic disease, but he could not confirm this opinion. His diagnosis was intestinal indigestion. After an oil test meal 45 c.c. of greenish fluid was aspirated which proved to be free from trypsin by Volhard's test. In these four cases the method seemed not only to give no assistance in the diagnosis, but even to be more or less inconsistent with the clinical findings.

CASES 5 and 6.—In two cases of cancer of the stomach, strongly positive results were obtained by the Volhard test: in the first 32.8, in the second 29.7. In neither case was there any pyloric obstruction since in one the orifices were not involved, while in the other a partial gastrectomy had been performed. It has been suggested that there is a vicarious digestion in the stomach by means of trypsin in cases of impaired digestion. Strange to say, however, there was no reduction of the gastric activity in either of these cases.

The three remaining cases show nothing of interest and may be given in Table 4.

TABLE 4.—OIL TEST MEAL AND VOLHARD'S TEST IN THREE CASES

Case.	Diag.	Quantity.	Color.	Volhard reading.
7	Chronic gastritis, with anacidity.	Small amt.	White.	4.0 (control water).
8	Hyperacid gastritis.	60 c.c.	Clear green.	0.0
9	Gastric ulcer.	250 c.c.	Green.	16.8

Oil juice was found active by Volhard in 9 out of 11, by Faubel in 23 out of 37, by Lewinski in 19 out of 27, by Molnár in 48 out of 50 cases. Boldireff, in a dog, was able to demonstrate the presence of trypsin before tying, and its absence after tying the pancreatic duct. Hemmeter and Lewinski found trypsin absent in the duodenal contents in cases of obstruction of the bile duct due to stone. Volhard, in a case of pancreatic diabetes, was able to verify the diagnosis of atrophy of the pancreas. He also found trypsin in two cases and was thus able to exclude pancreatic disease, which had been

suspected. In 22 cases of achylia he missed trypsin only once. He found the same to be true of subacidity, and believes that this offers a plausible explanation of the good peptonization observed in these cases.

CONCLUSIONS

1. The duodenal contents may frequently be obtained after the oil test meal, though sometimes there is doubt as to the character of the fluid aspirated.

2. On this account it may be possible to exclude atrophy of the pancreas, but only under very unusual conditions can we demonstrate its presence. In a number of diseases the examination has yielded suggestive results.

3. The observation of Boldireff is of more interest from the point of view of pathologic physiology than of diagnosis, for example, in gastric ulcer and in achylia.

4. The casein method of Volhard is a delicate qualitative test for trypsin, but for this purpose needs simplification.

5. The regurgitation of the alkaline intestinal juice induced by oil may explain the therapeutic value of the latter in some cases of hyperacidity.

Finally, I desire to express my thanks to Dr. Robert G. Torrey for aid in performing the tests.

REVIEW OF LITERATURE

Boas: Centralbl. f. klin. Med., 1889, No. 6, x, 97; Ztschr. f. klin Med., 1890, xvii, 155.

Tschlenoff: Cor.-Bl. f. schwerz. Aerzte, 1889, No. 6, xix, 161.

Boas described the first systematic method for obtaining the duodenal contents. His plan was to massage the abdomen in the region of the gall-bladder and left lobe of the liver and afterward to aspirate any fluid that might have been forced into the stomach. In about fifty cases he obtained active intestinal juice in which he was able to demonstrate amylolytic, lipolytic and proteolytic ferments. He states that the tryptic action of the pancreatic secretion in weak acid or alkaline solutions is the only decisive test. He gives a complete description of the duodenal contents, which holds good for the fluid obtained by the oil method.

Tschlenoff was able to obtain intestinal juice in five out of seven patients by the Boas method.

Hemmeter: Arch. f. Verdauungskr., ii, 85.
Kuhn: München. med. Wchnschr., 1896, No. 29, p. 674.

Hemmeter asserted that he was the first to introduce a methodical procedure for obtaining the duodenal contents by intubation of the duodenum. Kuhn's instrument is much simpler and better than Hemmeter's but either one requires too much technical skill to admit of its general use in clinical diagnosis.

Einhorn: New York Med. Jour., 1908, No. 25, lxxxvii, 1179.

Einhorn has modified his "bucket" for the purpose of obtaining the contents of the duodenum for examination.

Goldschmidt: Deutsch. med. Wchnschr., 1909, No. 12, xxxv, 522.
Gross: Ibid, 1909, No. 16, xxxv, 706.

Goldschmidt and Gross, using the latter's method for detecting trypsin, have recently discovered this ferment in the feces of all normal persons examined. This does not agree with the observations of previous writers, but if confirmed will render the use of oil test meals quite superfluous.

Boldireff: Zentralbl. f. Physiol., 1904, No. 15, xviii, 457; Centralbl. f. Physiol. u. Path. d. Stoffwechs., 1908, No. 6, viii; Arch. f. d. ges. Physiol., 1907, Part 1, cxxi, 13.

The following is a condensation of Boldireff's most important conclusions. After fatty food, in cases of excessive acidity, and after long-continued fasting, a mixture of the pancreatic, intestinal and hepatic secretions pours into the stomach. This fact is utilized to obtain pancreatic juice and bile for examination, and must also be taken into account in tests to determine the acidity, the ferments and the motility of the stomach. Boldireff believes that when fatty food is taken gastric digestion is carried on largely by the ferments of the pancreas. He also states that none of the hypotheses which have been proposed to explain the fact that the stomach does not digest itself take the reflux of pancreatic juice into account. He thus hints at a new theory for the explanation of gastric ulcer. Hyperacidity does not increase the peptic power of pepsin but does favor regurgitation of pancreatic ferments.

Volhard: München. med. Wchnschr., 1907, No. 9, liv, 403.
Faubel: Beitr. z. chem. Physiol. u. Path. (Hoffmeister), 1907, x, 35.
Löhlein: Beitr. z. chem. Physiol. u. Path. (Hoffmeister), 1906, vii, 120.
Molnár: Ztschr. f. klin. Med., 1909, Parts 1-3, lxvii, 188.

Volhard was the first to employ Boldireff's plan for clinical purposes. For testing the "oil juice" he modified his pepsin method. The casein solution required is prepared as follows:

One hundred gm. of finely granular casein are added to 1 liter of distilled water treated with 80 c.c. of normal sodium hydroxid and made up to 2,000 c.c. with chloroform water. The mixture is slowly warmed on the water bath, with frequent shaking, till all the casein is dissolved, and then quickly raised to 85 or 90 C. to destroy bacteria and ferments. After cooling, a layer of toluol is added to prevent access of bacteria.

An individual test is carried out as follows:

One hundred c.c. of casein solution are placed in a flask marked at 300 and 400 c.c.; chloroform water is added to the mark 300 and then an accurately measured amount of trypsin solution (5 or 10 c.c.) previously neutralized. (The acidity may, however, be noted in advance and the necessary corrections made after the final titration.)

Control flasks are prepared in a similar manner, distilled water taking the place of trypsin solution. After incubation for a definite period of time, 11 c.c. of normal hydrochloric acid is added to each flask and then complete precipitation brought about by filling the flasks to the 400 c.c. mark with 20 per cent. sodium sulphate solution. After complete filtration 200 c.c. of the filtrate from each flask is titrated with decinormal sodium hydroxid solution, using phenolphthalein as an indicator. The acidity of the control is subtracted from that of the ferment containing solutions. In my tests the only modification of this method was in the use of a different preparation of casein from that recommended by Volhard (not obtainable in this country) and in the use of half the quantities recommended by him (Merck's Casein [Hammarsten] was used). My results were multiplied by two so as to compare with the results of other writers. Volhard and his followers found that trypsin as tested by this method did not follow the Schütz-Borrisow law.

Gross: Arch. f. exper. Path. u. Pharmakol., 1907, Parts 1-2, lviii, 157.

Lewinski: Deutsch. med. Wchnschr., 1908, No. 37, xxxiv.

Lewinski used the oil method in 27 cases, using the Gross test to detect the presence of trypsin. At first he was unable to obtain trypsin in hyperacidity cases, but afterward by giving half a teaspoonful of magnesia before the oil and again in twenty minutes, he was uniformly successful. He thinks that failure to obtain active juice shows pancreatic insufficiency or mechanical interference with the passage of the pancreatic secretion into the stomach.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. STOCKTON, CRANE AND FARR

DR. G. E. PFAHLER, Philadelphia: We know so little that is definite in the diagnosis of cancer of the stomach that everything in advance in this line must be welcomed by all. If the members of the section will examine the plates which Dr. Crane has so carefully prepared, and which may be seen in the scientific exhibit, they will be convinced that the *x*-ray is not an illusion, but gives evidences of cancer. I have seen 35 cases of carcinoma of the stomach; some came to autopsy, while in the others the patients came to operation. In the majority there was no palpable tumor present. In the cases in which there was a palpable tumor it had to be differentiated from tumors of some other part of the intestinal tract. Very valuable evidence is given in this line by the *x*-ray. I think that the sooner the medical man gets in mind the actual and true position of the normal stomach, and forgets what has been considered as classical, the sooner will we enter lines of progress. It is hard to convince a man who is not familiar with the *x*-ray of its value in these cases. As a matter of fact, only one-half the evidence is obtained by the *x*-ray plate; the other half is obtained on the flouroscopic screen. Movements, such as the peristaltic movements, are not revealed on the plates, and I think these form the basis of a positive diagnosis, an early diagnosis. A little induration in the stomach walls, especially if occupying the lesser or greater curvature, causes a change in the wave, but this evidence cannot be obtained on the plate. Of course, a study of the plate by an experienced man is important.

I believe that unless we apply the pain-marker over the seat of pain and move the stomach, to determine that the point of pain moves with the stomach, it is of not much value. I think evidence found at autopsy will bear me out in this.

One must examine these patients in at least two positions, both the vertical and the recumbent. If in the vertical position with proper manipulation, moving the patient sideways, working on either side of the spinal column, will bring out all the evidence that is possible. I have been using bismuth subcarbonate and find it entirely satisfactory. In an examination of 365 patients for conditions affecting the gastrointestinal tract, in whom I used from 2 to 3 ounces of bismuth subcarbonate, I found no toxic symptoms, or a single symptom that could be traced to the use of the bismuth. I think this is a perfectly safe method. The only objections I can see are that too much time and patience are required and, also, one is put to a considerable expense. But these objections can be overcome.

DR. A. W. CRANE, Kalamazoo, Mich: One caution occurred to me in drawing conclusions from stomach contents obtained at different levels by the stomach tube. This is illustrated by

one *x*-ray plate in the scientific exhibit on Young's Pier taken with the stomach tube in place in the stomach. It may there be seen that the cardiac orifice is on the side and not on top of the stomach. This orifice passes into the stomach toward the upper part of the great curvature. In many cases the end of the tube stops there, as shown by the skiagraph. If a further introduction of the tube is attempted the tube bends; the point does not descend. This is true in a certain proportion of the cases. In this particular plate it is determined beyond a doubt. In many cases in which the stomach contains but little, the contents can be obtained by placing the patient on his back in nearly a horizontal position; then the stomach contents flow upward to the fundus and can be easily drawn off with the tube. Again, in the so-called hour-glass stomachs, when there is a constriction between the upper and lower sacs, the opening is generally too small to permit the passage of the tube. In these cases the stomach contents are obtained from the upper sac, and would not differ in any respect from the contents of an esophageal diverticulum. I doubt if any man can tell whether the end of the tube is in the upper sac of an hour-glass stomach in which the constriction is high up, or in a diverticulum. The attempted diagnosis of such conditions with a stomach tube is open to serious objections. The *x*-ray plate is necessary.

Dr. Judson Daland, Philadelphia: During the past three years I have seen a number of cases of gastric tumors studied by *x*-ray, and it seems to me from the experience gained that so far as gastric carcinoma is concerned the entire work is in its very beginning. At the same time, we must acknowledge that the *x*-ray does aid us materially and in many directions. Often it makes clear the position of the tumor, whether gastric or not. It seems to me that it is especially important to be able to determine the peristaltic waves, if they can be plainly and distinctly seen. I believe that the flouroscope has a value of more than one-half that of the skiagram. By the use of the screen one obtains, on the whole, more information than can be obtained by the skiagram. However, both methods must be employed. The use of bismuth in *x*-ray work is a welcome addition to diagnosis, and all the work that is to be done should be done with as much enthusiasm as has been shown in the past. By paying more attention to the work more definite signs than we now possess will be brought out. We need much more *x*-ray evidence than we now possess, and we must acknowledge that we have little evidence of carcinoma of the stomach, particularly in the early stages, when a diagnosis is most important. The use of the subnitrate of bismuth in doses of from 2 to 3 ounces for *x*-ray work I have seen give trouble which was of no particular importance; there would probably be a gastrointestinal irritation for two or three days and then it would pass away. Its occurrence was

rather unusual and therefore did not constitute a bar to the further use of the *x*-ray. I think the subcarbonate is to be preferred to the subnitrate of bismuth.

DR. ALLEN A. JONES, Buffalo: It is misleading when one attempts to judge the position and size of the stomach by means of the stomach tube; one cannot say that he is dealing with a normal stomach, a stomach in a normal position and of normal size, when the tube is used for this purpose. The contents may come through the stomach tube anywhere from nineteen inches or lower, even to twenty-six inches in normal cases. The contents may be obtained from the fundus or from the pyloric extremity. I was interested in Dr. Crane's statement in regard to hour-glass contraction of the stomach; he found it was impossible to differentiate between the contents obtained from the fundus and that obtained from a diverticulum of the esophagus, from a dilated esophagus, or from a stenosis from any cause. This emphasizes the extreme importance of the pyloric region of the stomach. Unless there is a proper mixture of gastric juice with the food at the pyloric extremity of the stomach, the stomach content does not assume normal characters. One point that Dr. Stockton mentioned was of considerable interest; this was the condition of the emptying function of the stomach with achylia gastrica. Recently considerable interest and significance has been attached to the chemistry in the duodenum and the pyloric closing and opening. It has been taught that, in normal digestion, when the duodenal contents reach an acid point, that is, a certain degree of acidity, a reflex action occurs which results in the closure of the pylorus, and no more contents are allowed to pass on until that which is already present is neutralized and has probably passed down further in the duodenum. If that is true, theoretically the passage of the gastric contents must be much hurried in achylia gastrica. But clinically such is not the case. We frequently find the contents retained in the stomach as long as would obtain in normal digestion. These are the cases in which we are apt to have symptoms of achylia gastrica. Peristalsis is, after all, the most effective measure, or means, of emptying the stomach contents into the duodenum, provided there is no pyloric stenosis and regardless of the fact that there is a low gastric acidity. On the contrary, however, it is in achylia gastrica that many marked cases of pyloric insufficiency and hurried emptying are observed.

DR. JOHN A. LICHTY, Pittsburg: At the risk of being considered a psychiatrist, I wish to call attention to the effect of the mind or nervous system on these patients in whom we think it necessary to use a stomach tube. I believe that in the first days that the stomach tube is used the findings are of very little value, especially if the patient is a nervous one. If you tell the patient that you will pass the stomach tube on him next day he will worry all night about it, wondering how

the stomach tube is going to feel. It certainly does have some effect on the digestive secretions, so much so in fact that the findings are of little value. I have also proved this in dogs. In our experiments on dogs we found that the dogs became fond of their keepers and the keepers could pass the stomach tube without any difficulty whatever; in these cases the stomach contents were found to be constant and normal. But one day one of the students asked me to let him go down and assist the janitor. All the dogs then had either diarrhea or vomited. This influence of the nervous system is not more so in dogs than it is in human beings. I wish to emphasize a point that Dr. Jones has mentioned in regard to the use of the *x*-ray, that is, the *x*-ray findings. Unless the stomach tube is passed up toward the pylorus the secretion withdrawn is not going to give a definite idea of the gastric secretion; one cannot always be sure of it. However, if the patient takes the tube nicely and easily, the physician then can rest assured that normal gastric secretion has been obtained. In spite of all this, I doubt whether the findings are always correct and that we can always make a correct interpretation of the findings. In those cases in which we have a definite clinical history we should disregard the gastric findings if they do not agree with the history. One should study the clinical history as much or more than the gastric findings.

DR. HENRY R. HARROWER, Chicago: I believe that there is a possibility of mistake regarding the finding of the Oppler-Boas bacillus which the text-books lead us to believe is pathognomonic of gastric carcinoma. I have been misled in my brief experience by finding them in a number of gastric analyses; they were undoubtedly Oppler-Boas bacilli, but no malignancy was associated with them at all. At least two years have passed in one case, and this patient is not suffering from any gastric disturbance whatever. I have in mind a man who was suffering from some serious stomach disorder which was diagnosed as cancer. He vomited practically everything that passed into the stomach and was dying of starvation. I made a careful examination of the gastric contents and found a large number of what I believe to be Oppler-Boas bacilli. I think these bacilli can be easily recognized after one has seen them a few times. This patient was treated with ordinary digestants and eventually gained seventy pounds; in a year he was perfectly well. The Oppler-Boas bacillus is not pathognomonic of gastric carcinoma and this should be emphasized more, and the statements made in some text-books should be changed.

DR. JOHN N. UPSHUR, Richmond, Va.: I do not think that there is a more interesting subject than the study of stomach troubles. I am satisfied that the best men are sometimes in error as a result of their conclusions the result of analysis of gastric contents. If they could find it possible to be at both

ends of the tube at the same time, that is, be the patient as well as doctor. I was one of those unfortunate people who had serious stomach trouble. I consulted several stomach specialists, who studied my case carefully. But I found from my own experience that my trouble was a neurasthenic one; it was a dilatation of the stomach of five inches, the result of a deficient motility as the result of a nervous breakdown. Four years later a specialist, who was thoroughly competent, told me that I had no dilatation at all. Now an exceedingly interesting thing to me was the use of the stomach tube. I am sure that I passed the stomach tube on myself at least 2,000 times. For seven years it was impossible for me to have a quiet night and be fit to work on the following day unless I used one gallon of sterilized water before retiring. The interesting feature in my case was that the digestive disturbance always came at the end of the day, when I was tired, mentally and physically. I am satisfied that the benefit, a decided benefit, arose from the use of the tube by causing a stimulation of the stomach with the sterilized water as a massage. The water was used at a temperature that was comfortable. There was an improvement in the motility of the stomach caused by the stimulation of the lavage together with long continued use of strychnine. I have not used the stomach tube for eighteen months and I am now in better physical condition than I have been in ten years and can do as much work as a young man can. What I wish to emphasize is that the best men are apt to make mistakes unless they can put themselves at both ends of the tube at the same time, at one end as the doctor, at the other as the patient; then they can arrive at some definite conclusion.

DR. C. URBAN SMITH, Baltimore: I agree with the statement that the presence of the Boas-Oppler bacillus is not positive of carcinoma of the stomach. From what has been expressed here to-day one would infer that its presence was of positive diagnostic value, but we frequently find the bacillus in benign conditions. There is no doubt but that the Gram-positive finding of the bacillus in the feces is a valuable link in establishing a positive chain of evidence. In regard to the withdrawing of the stomach contents, and the statement that all the contents are rarely obtained by the ordinary methods, I wish to say that I find the expression method which is used largely in Germany is probably the best and simplest method to completely empty the stomach when properly performed, but requires a certain amount of practice and experience.

DR. FRANK SMITHIES, Ann Arbor, Mich.: Dr. Stockton should be praised for the complete résumé that he has given us. It seems to me that a fact not strongly emphasized should be mentioned. In the examination of stomachs the tube is frequently passed without sufficient attention being given to the state of the patient's mouth and teeth. Before the tube is

passed it is well to have thorough cleansing of the teeth, mouth and throat. I recently had an experience which strongly impressed this on me. A specimen supposed to be Oppler-Boas bacillus was sent to me. It turned out to be leptothrix from a dirty mouth. I think that greater stress should be laid on frequent examinations of the gastric secretions and contents. Outside of institutions it is common to have a diagnosis offered a patient, based on but one stomach examination. As Dr. Lichty has pointed out, this amounts to but little unless the findings are positive ones, as, for example, the contents showing atypical cells, bacilli, etc., at this examination. With respect to the *x*-ray evidences in the diagnosis of cancer of the stomach, I must frankly admit that "I am from Missouri." From a somewhat careful examination of the plates submitted, I must say that I see little that would lead one to differentiate between early cancer or ulcer. And it must be remembered that it is in the early cases that we are justified in recommending refinements of diagnosis. A study of the abdomen with the aid of a fluoroscope frequently tells us important things respecting gastric and intestinal motility. But I fail to see that the *x*-ray offers any more information or more exact information than one can gain from careful examination with the aid of the stomach tube at appropriate sittings. And it should be emphasized that the stomach tube is always at hand.

DR. ALEXANDER LAMBERT, New York: Has Dr. Crane noticed in the skiagraphs of cancer of the stomach any relation between the pain described by the patient and the tenderness as elicited by the examination? As we know, the abdominal viscera refers pain to the abdominal wall. Has he drawn any conclusions; is there any relationship between the place of pain, as described by the patients, and the seat of the lesion as elicited by *x*-ray examination in cases of gastric carcinoma?

DR. PHILIP KING BROWN, San Francisco: It is not an easy matter to differentiate the Boas-Oppler bacilli, and it cannot be done positively by simple staining methods. There are two definite types of organisms closely resembling the Boas-Oppler bacilli, and found commonly in stomach contents and stool. One is not uniformly positive with the Gram stain and has the same morphology as the colon group; Schmidt calls it the pseudocolon type. The other is very difficult to differentiate from the Boas-Oppler bacillus in stained specimens, except that it is slightly larger and thicker, and appears in long chains in the stool. It is also Gram-positive. What Dr. Smith has said is true; but be certain you are getting the Oppler-Boas bacillus before telling the patient that he has cancer.

DR. CHARLES G. STOCKTON, Buffalo: Hour-glass stomachs are not seen frequently; it is not a common condition. A stomach tube could not pass through such a constriction readily, although I have done it in two cases. I feel convinced that the statements I have made will stand, with some excep-

tions of course. What Dr. Jones has stated in regard to the distance of the tube is perfectly true. Dr. Lichty's statement regarding the mental impression on the gastric secretions is correct and I am glad that he emphasized it as he did. The conclusions drawn regarding the stomach condition from one or two examinations are often misleading and throw the practice into disrepute. As to the Oppler-Boas bacilli, I think what has been said is true, but it has been said more strongly than I would say it. These bacilli are found in conditions not cancerous, but not in such abundance or regularity that I imagine one would believe from hearing what has been said. They are not at all pathognomonic of cancer. But when they are found in abundance they certainly have a diagnostic bearing, especially when taken in connection with other findings. Their presence does not stand alone and by itself in the diagnosis of cancer; this has never been claimed for them.

DR. A. W. CRANE, Kalamazoo, Mich.: If I gave the impression that the *x*-ray was an infallible means of diagnosticating cancer of the stomach, it was a mistake; it is simply one added factor to the other methods we have. To make plates is comparatively easy, but to interpret them requires understanding and training. To recapitulate briefly, the *x*-ray evidence of cancer of the stomach lies in the deformity of the normal outlines of the stomach. Ulcers or the scars of ulcers give contractures, while cancer gives an indentation of the stomach-wall. These distinctions are illustrated by many plates in the scientific exhibit. I should like to ask, and with a great deal of feeling, that the medical men give more attention to what the *x*-ray men in this country have to show them. They will find something in this method of diagnosis applied to the stomach.

TRANSMISSION OF MALARIAL FEVER IN THE CANAL ZONE BY ANOPHELES MOSQUITOES

SAMUEL T. DARLING, M.D.
ANCON, CANAL ZONE

It is between eleven and twelve years since Ronald Ross conducted his famous experiments demonstrating the transmission of malarial fever by mosquitoes. This demonstration, it seems to me, has contributed more to the forging of the key to the control of the tropics than any other one in the annals of tropical medicine, for Ross' discovery focussed the attention of the medical world on the part played by suctorial invertebrates in the transmission of infectious diseases. Knowledge of this doctrine of the insect intermediary host, coupled with Dr. H. R. Carter's invaluable observation of the extrinsic period of incubation, enabled the yellow fever commission to verify Finlay's notion about the transmission of yellow fever by stegomyia mosquitoes.

The application of these two discoveries, Ross' and Reed's, to the problems of preventive medicine by your President-elect has made yellow fever a historic disease in Panama and is surely reducing the morbidity and mortality from malarial fever to the vanishing-point.

The object of the work briefly reported here was to go over the whole subject of the transmission of malarial fever by anopheles mosquitoes. I have been guided by the work of Ronald Ross, Stephens, Christophers and James, whose investigations of malaria in India and Africa must stand as models for all future workers on this subject. In every malarial region it is a matter of

importance to determine the varieties of anopheles in that region, their bionomics, the species hospitable to malaria and those which can not transmit it. The English investigators, James, Christophers and Stevens, observed that different species of anopheles had different degrees of susceptibility to malaria; certain species were natural transmitters of malarial fever, while others were rarely, if ever, found infected naturally, although it would be possible to infect them under laboratory conditions. It is important, then, to determine what varieties of anopheles are present and which ones may act as the intermediary hosts in the transmission of malarial fever; this is particularly true when the malaria-transmitting anopheles have different breeding habits from those which are not responsible for the spread of malarial fever. Various observers have published notes on the breeding habits of anopheles. It may be said that there is as much selection of breeding-places by anopheles as there is selection of feeding-grounds by fish. Trout, salmon and bullheads have their analogues among anopheles larvæ, some requiring fresh aerated water, or water containing much green algæ; others select tree-holes and the recesses of epiphytic tree-plants, such as bromelias, as breeding-places; while others preferring fresh aerated water are so adaptable that they will breed in brackish water, containing half its volume of sea-water; some species require plenty of sunlight, while other sylvan species prefer shady pools in which chlorophyl-bearing algæ are relatively absent.

The identification of mosquitoes used in these experiments has been corrected or verified by Mr. A. H. Jennings, and his identifications are being checked in the Bureau of Entomology, U. S. Department of Agriculture, Washington.[1]

1. Dr. H. G. Dyer, has since verified all our identifications save one rubbed specimen which is probably *A. apicimacula*.

Notes on the species of anophelines in the Canal Zone, their relative numbers and breeding habits, were published by Mr. August Busck of the U. S. Bureau of Entomology in May, 1908. Eleven species of anophelines have been collected in the Canal Zone. Of these eleven species the three commonest ones are *A. albimanus, A. pseudopunctipennis* and *A. malefactor. A. albimanus* is much the commonest anopheles in the Canal Zone and is the one oftenest taken in quarters and barracks, although the proportion of one species to another varies somewhat with the season and locality. In certain villages only *A. albimanus* is taken in barracks, while in other villages from 5 to 10 per cent. will be *A. pseudopunctipennis,* and at Ancon during October, 1908, 27.5 per cent. were *A. malefactor* and 72.5 per cent. were *A. albimanus.* Tree-breeding species are rarely encountered and I know of no instance in which specimens of this species have been taken in quarters. The female anopheles visits quarters to obtain blood, which is necessary for the development of her ova. When specimens of *A. albimanus* (males and females), placed in a large comfortable breeding-jar with sufficient vegetable food, such as dates and bananas, were permitted to pair, the ovaries of the females showed no development within fifteen days.

The experiments were begun in October, 1908, during the rainy season and discontinued in February, 1909, during the dry season. Mosquito larvæ were collected by sanitary inspectors at various places in the Canal Zone. On being received at the laboratory, larvæ and algæ were placed in moist jars on a table in front of a window with an eastern exposure so that they got direct sunlight for an hour or two in the morning. Predaceous larvæ were killed and removed from the breeding-tanks. A preliminary difficulty was experienced in the gradual fouling the water of the tank; this was obviated in a very simple way by passing air bubbles through the water with a Paquelin cautery bulb. In

this way the water was kept fresh and the larvæ remained vigorous. After the larvæ had pupated they were placed in breeding-out tubes plugged with cotton, and after twenty-four or forty-eight hours the newly emerged mosquitoes were transferred to jars made of lantern chimneys, covered with crinoline gauze, where they might pair and be kept for biting. Females would bite twenty-four to forty-eight hours after emerging; frequently on successive and always on alternate nights for a period of at least fifteen days. The species of anopheles used were *A. albimanus, A. pseudopunctipennis, A. franciscanus, A. argyritarsis, A. malefactor* and *A. apicimacula.* These mosquitoes fall into three groups: the white hind-footed group; the uniformly colored group; and the spotted-legged group.

A series of bitings were conducted on suitable infected patients who were carrying estivoautumnal or tertian gametes in their peripheral blood, using four varieties of mosquitoes. Out of several hundred mosquitoes used in the biting experiments, 100 mosquitoes were dissected, and of these 70.8 per cent. of *A. albimanus* became infected; 12.9 per cent. of *A. pseudopunctipennis* became infected, and none of *A. malefactor* (17 mosquitoes used) became infected, although several of the latter were purposely placed in jars with *A. albimanus* and bit at the same time persons from whom the specimens of *A. albimanus* became infected.

It is concluded from this series of biting experiments that *A. albimanus,* the common white hind-footed mosquito—an extremely hardy, vigorous, rapidly developing, adaptable mosquito—is the transmitter of estivoautumnal and of tertian malarial fever in the Canal Zone at this time. Specimens of this species infected with tertian parasites became infective between nine and eleven and a half days after the first feeding. When infected by estivoautumnal parasites, sporozoites appeared in the salivary glands as early as the eleventh day in some mosquitoes and later than twelve and a

half days in others. *A. malefactor* is not concerned in the transmission of malarial fever in the Canal Zone at this time. *A. pseudopunctipennis* is only slightly concerned in the transmission of malarial fever; this appears not only from the fact that only four out of thirty-one mosquitoes under the most favorable artificial conditions became infected, but from the additional fact that relatively few specimens are taken in quarters at the present time.

The English investigators appear to have made no attempt to determine the limits of infectiousness of man in malarial fever. To me this appeared to be, if possible, worth determining, because in the discharge of patients from the hospital it would be manifestly unwise to turn a patient out, although free from symptoms, yet with gametes enough in his peripheral blood to infect every susceptible anopheles mosquito that might bite him. Efforts to determine the limit of infectiousness of man were made in the following way:

In the 47 biting experiments, several blood preparations were taken fresh and for staining, at the time of the biting. Differential counts of leucocytes and the ratio between crescents and leucocytes were determined the next morning. Leucocyte counts were occasionally made at the time the blood was taken so as to check this method of estimating the crescents. In this way it was always known how many crescents were in the peripheral blood per c.mm. at the time the mosquito was infected. The next step was to weigh a number of mosquitoes before and after biting in order to estimate the amount of blood retained by a mosquito. In this way the approximate number of gametes ingested could be calculated. Again, smears were made from the midgut of mosquitoes that had a few minutes before bitten a person whose blood contained numerous gametes. From this it was found that about one-half the gametes were phagocyted by polymorphonuclear leucocytes and thus destroyed. Finally, mosquitoes which had fed but once

on patients whose crescents per leucocytes had been estimated were fed subsequently on dates, and on dissection of these mosquitoes the probable limit of infectiousness was determined as being near one gamete per 500 leucocytes. From these observations, I am confident that a patient with more than one crescent for every 500 leucocytes, or 12 crescents per c.mm., is infective, and it follows that such an individual should not be discharged from treatment in that condition or should be warned or required to continue treatment. Such a person is a gamete-carrier and is a menace to a malarial community whenever susceptible anopheles have access to him.

The effect of quinin administration on the number of gametes in the peripheral blood was studied in a number of patients suffering from estivoautumnal and tertian fever by the administration of 30 grains quinin daily, either with or without iron and arsenic, and by withholding quinin and merely requiring rest from labor. In estivoautumnal infections, when there were crescents in the blood, the number was reduced by quinin, 30 grains daily, at the following rates. For example, in Experiment 17 there were:

9 crescents per 100 leucocytes on December 26
5 crescents per 100 leucocytes on December 27
5 crescents per 100 leucocytes on December 28
4 crescents per 100 leucocytes on December 30
1 crescent per 100 leucocytes on December 31
0 crescents per 100 leucocytes on January 2
0 crescents per 100 leucocytes on January 13

In Experiment 20 the crescents were reduced from 67 per 100 leucocytes to one per 200 leucocytes in twenty-five days.

In Experiment 41 crescents were reduced from 92 per 100 leucocytes to one per 100 leucocytes in fifteen days; while, on the other hand, in Experiment 6, when quinin was withheld, crescents remained constantly in the peripheral blood for twenty-three days, there being

16 crescents per 100 leucocytes on admission and 20 crescents per 100 leucocytes at the end of the period.

From this it is concluded that generous daily doses of quinin, grains 10 t. i. d., will reduce the sexual forms of the estivoautumnal parasite to a non-infectious minimum in from a few days to two or three weeks, depending on the severity of the infection.

In tertian malarial fever there is never an abundance of gametes in the peripheral blood after the disappearance of the asexual forms such as is seen in estivoautumnal infections; besides, all forms of the tertian parasite disappear from the peripheral blood within two or three days under quinin treatment and occasionally disappear when quinin is withheld.

A curious relation was observed between the average number of days that gametes remained in the blood in estivoautumnal and tertian infections when under quinin treatment, the number being about ten in estivoautumnal and three in tertian, and the average proportion of the incidence of estivoautumnal to tertian malarial fever in the Canal Zone. This might be interpreted as indicating that the proportion of cases of estivoautumnal to tertian malaria depends on the number of days that gametes are in the peripheral blood in numbers sufficient to infect *A. albimanus,* which is the host for both forms of the parasite.

The infection of *A. albimanus* and the development of malarial parasites in her midgut is not interfered with by quinin when such an infected mosquito feeds daily or on alternate days for fifteen days on patients who are receiving 30 grains of quinin in solution daily. In these instances the zygotes mature and sporozoites reach the salivary glands in the usual period.

Observations on latent malaria were made during the past dry season in several villages where the malarial sick-rate did not fall to zero and where no anopheles were breeding. On a systematic blood examination of laborers and their families, I found that 10 per

cent. of men who were at work without symptoms had parasites. Three per cent. of the cases of latent malaria were of the estivoautumnal variety and 7 per cent. of the tertian variety. Among the families of Spanish and West Indian laborers the amount of latent malaria was 30 per cent. A few cases of fever would arise from this source every week, probably following some loss of resistance caused by dissipation, wetting or overheating. It is this latent malaria in every tropical community which contributes largely to the preservation of the malarial parasite and to the infection of anopheles when, after the onset of the rainy season, mosquitoes have begun to breed in numbers.

The theories of Mannaberg and Craig explain the persistence of latent malaria by the process of conjugation of two ring forms within a red blood corpuscle. During examinations of the blood, in cases of latent malaria, I have frequently seen estivoautumnal crescents which had apparently been formed by the fusion or conjugation of two ring forms, or of two pigmented forms, but I have also very frequently seen in estivoautumnal and tertian malaria red blood cells infected by two or more ring forms which have gone on to maturity without conjugation. Sometimes these contiguous parasites were of the same age, but oftener one would be a little older.

Quinin administered in latent malaria appears to destroy the ring forms only and prevents the possibility of their development into gametes. The gametes in the blood stream are probably phagocyted by splenic and hepatic endothelial cells and are not influenced by quinin directly.

The points I wish to emphasize are these:

A. albimanus, the common white hind-footed anopheles, is the host for estivoautumnal and tertian malarial parasites in the Canal Zone at this time.

A. malefactor, notwithstanding its name, does not transmit malarial fever.

A. pseudopunctipennis is only slightly concerned in the transmission of malarial fever.

In the efforts at mosquito destruction, the extermination of *A. albimanus* is of paramount importance.[2]

Patients having crescents or tertian gametes in their peripheral blood should not be discharged from the hospital, nor should treatment be discontinued until gametes have been reduced to a non-infectious minimum. The destruction and prevention of development of the sexual parasites in man is of great importance and may be accomplished (1) by appropriate quinin treatment of all gamete-carriers entering the hospital; (2) by occasional quinin treatment to destroy latent malaria; (3) by the periodical blood examination of laborers in quarters where there is a high malarial rate for the detection of gamete-carriers and latent malaria in order to carry out appropriate treatment.

Thirty grains of quinin sulphate in solution daily is an efficient dose for the purpose required.

Ancon Hospital.

ABSTRACT OF DISCUSSION

DR. JOHN A. WITHERSPOON, Nashville, Tenn.: We all know now that the malarial parasite is really carried by the mosquito. I have been especially interested in the attacks made on the anopheles in the Canal Zone and the special methods used. It seems to me that the great work in the Canal Zone, especially in carrying out the discoveries of Ross, means much for the future, not only for the preservation of life of the people, but for the natural resources of the country. It solves the problem of what to do with the products of that country; it solves the problem of how the Canal Zone can be peopled. Nothing could be accomplished without these important discoveries. I think the people owe a debt of gratitude not only to Colonel Gorgas, but to men like Dr. Darling and others who are working there every day. The excellent work that is being done in the Ancon hospital is a credit to any country; the work done in the Canal Zone is a credit to the nation.

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2. I have since determined that *A. tarsimaculata* also transmits estivoautumnal parasites. This mosquito belongs to the white-hind-footed group and has recently been breeding in rather large numbers in brackish water near Colon.

DR. SEALE HARRIS, Mobile, Ala.: It seems to me that we should apply the lessons learned in the Canal Zone to our own country. The majority of us who treat malaria cease giving quinin after the patient has been relieved of his fever. In order to prevent other mosquitoes becoming infected, I think it would be well to continue the use of quinin for a considerable length of time. Note the antimalarial work that has been done in Italy in the last five years; the death-rate there from malaria has been reduced two-thirds by this crusade, which was carried on with the idea of preventing the mosquito becoming infected. After the patients were free of fever for some days, after a sufficient dose of quinin had been given to relieve the paroxysms, quinin is given in small doses, 6 grains a day, for a period of at least three months. It seems to me that in the treatment of malaria we should use exactly the same methods to prevent others from becoming infected, as with patients afflicted with yellow fever. Malaria and yellow fever are diseases, so far as their transmission is concerned, of much the same character. Both are transmitted by the mosquito. If we use the same measures in malaria as are used in Italy, I think we can reduce the number of cases of malaria very materially. In handling a patient with malaria, the first thing to do is immediately to isolate him by placing him under mosquito bar, or in a house where the mosquitoes cannot gain entrance. Individuals who have been exposed should receive prophylactic doses of quinin. The medical profession should begin an active crusade against malaria in this country. It means a great deal to us. When we consider that the number of deaths from malaria is probably 15,000 per annum and that several millions of people in the United States are affected by that disease, we realize the importance of the disease and we should at once institute a crusade against it. I am sure that such a crusade, carried out as it has been in Italy, will give results as good as have been obtained there.

THE ASSOCIATION OF AORTIC INSUFFICIENCY WITH SYPHILITIC AORTITIS

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During the last few years our attention at the Pennsylvania Hospital has been very forcibly directed at autopsy to the frequent association of a peculiar type of arteriosclerosis, namely, mesaortitis, with a chronic aortic endocarditis, which gave rise to aortic insufficiency. The combination of these two lesions seemed so significant and was so striking that a systematic study of the autopsy material was undertaken to determine exactly how common the occurrence was; and in this paper a brief summary of the findings will be given.

For some years mesaortitis has been recognized by the school of Heller as a unique form of arteriosclerosis, but more recently the condition has been made especially familiar and its connection with syphilis emphasized by the studies of Marchand,[1] Benda[2] and Chiari.[3] Chiari pointed out in 1903 that mesaortitis was very common in syphilitics. In his series of twenty-seven cases of undoubted syphilis, mesaortitis was found sixteen times, and in forty-four cases of paresis it occurred in 47 per cent. Marchand, at the same time, drew attention to the constant association of mesaortitis with aneurism of the aorta and believed that, though this type of aortitis might not be specific for syphilis, was yet almost always

1. Marchand: Verhandl. d. deutsch. path. Gesellsch., 1903, p. 197.
2. Benda: Verhandl. d. deutsch. path. Gesellsch., 1903, p. 164.
3. Chiari: Verhandl. d. deutsch. path. Gesellsch., 1903, p. 137.

caused by syphilis when it occurred in young people. Since the appearance of these papers the condition has been extensively studied and is now generally recognized as a type of sclerosis differing in appearance and etiology from the more usual form of sclerosis termed endarteritis deformans.

Evidence, too, has been rapidly accumulating to show that mesaortitis is due, at least in many cases, to syphilis. A similar lesion has been found by Wiesner[4] and Klotz[5] in the great vessels of infants and fetuses that were the subjects of congenital syphilis. Most important of all in this regard are the reports of Reuter,[6] Benda,[7] Schmorl[8] and Wright,[9] who have been able to demonstrate spiral organisms indistinguishable from *Spirochæta pallida* in mesaortitis in adults. It is interesting to note in Wright's excellent and convincing report that chronic aortic endocarditis was present in all of the five cases in which spirochetes were present in the wall of the aorta.

In a series of 930 autopsies at the Pennsylvania Hospital twenty-one cases were found in which chronic aortic endocarditis, unassociated with lesions of any of the other valves, occurred in connection with mesaortitis. In these twenty-one cases the lesions in the aorta varied somewhat in extent in the individual instances, but was always confined, and often very sharply localized, to the arch of the aorta. Occasionally it extended for only 5 cm. above the aortic cusps. The margin of the sclerotic area was very abrupt, while the aorta beyond was quite smooth. In the least extensive areas there were patches of thickening two to three cm. in diameter. The central portion was elevated, gray and somewhat succulent in appearance, while the margins were yellowish and crinkled. The sclerosis, when more extensive, was char-

4. Wiesner: Centralbl. f. Path. u. path. Anat., 1905, xvi, 822.
5. Klotz: Jour. Path. and Bacteriol., 1907, xii, 11.
6. Reuter: München. med. Wchnschr., 1906, liii, 10, 778; Ztschr. f. Hyg. u. Infectionskrankh., 1906, liv, 49.
7. Benda: Berl. klin. Wchnschr., 1906, xliii, 989.
8. Schmorl: München. med. Wchnschr., 1907, liv, 188.
9. Wright: Boston. Med. and Surg. Jour., 1909, clx, 539.

acterized by an irregular, corrugated or crinkled thickening of the wall, showing small pits and sometimes minute, aneurismal sacculations. Often the bases of these small aneurisms were so thin that they transmitted light. There was no calcification except in one instance, but rather a rubbery, pliable thickening. In four cases the arch of the aorta was the seat of large aneurism formations.

The valves showed the same rubbery thickening when extensively involved, and occasionally there were crescentic lines of whitish yellow thickening on the endocardium of the ventricle beneath the valves.

Microscopically these aortas showed even a more characteristic appearance than they did to the naked eye. The intima presented various grades of thickening, due to the heaping up of cells of the connective-tissue type, but there were no marked degenerative changes and no calcification. The principal alterations were present in the media. Here there were, in the great majority of instances, areas of necrosis in which both muscular and elastic elements were completely destroyed, while with occasional giant cells accumulations of small round cells and plasma cells were sometimes arranged about the necrotic areas. Usually blood-vessels, surrounded by these same types of cells, were seen penetrating from the adventitia far into the media toward the thickened intima. In other instances the media was the seat of old scar-like areas containing blood-vessels and the connective tissue was richly infiltrated with plasma cells and small round cells. In such places the elastic fibers of the media, as could be shown by Weigert and Verhoff stains, were entirely destroyed and the adventitia and thickened intima were connected by the vascularized scars. In the oldest lesions the media was represented simply by slightly cellular bundles of connective tissue. The adventitia likewise was the seat of definite changes. Here the connective tissue was increased; collections of small round cells were present, situated especially about blood-

vessels, the arteries were frequently the seat of an extensive endarteritis and the walls of the veins were thickened.

In three cases in which the valves themselves were studied microscopically this process was seen to extend to within a short distance of their attachment. At the fibrous ring there was increase in connective tissue. and blood-vessels could be seen extending from this region, while into the thickened valve near them accumulations of small round cells and plasma cells infiltrated the fibrous tissue of the ring. The valves themselves were thickened by the formation of fairly cellular connective tissue, and near the bases, in two instances, the valves were infiltrated with clusters of small round cells and plasma cells.

From this brief description it may be seen that the lesions in the aorta in these cases were quite characteristic of aortitis as it has been described by others. The process, moreover, could be traced along the wall of the aorta to the aortic cusps and, though, by reason of their structure, one could not expect to see the same type of lesion in the valves, still it was possible to determine that certain of the features characterizing mesaortitis were present here. The extension of blood vessels and groups of small round cells and plasma cells from the fibrous ring into the base of the leaflet, as well as the presence of small groups of these cells in the substance of the valve itself, was quite striking in at least once case, and, though this is not, by any means, sufficent to characterize the lesion in the valves as one of a specific nature, still it does suggest that the agent which produced the chronic inflammatory and proliferative changes in the wall of the aorta had some part in the disease of the aortic valve.

It is quite evident, too, that lesions of the aortic valve accompany mesaortitis with great frequency, for in another series of thirty-seven cases of mesaortitis, in which special attention was paid to the lesion in the aorta,

chronic aortic endocarditis with insufficiency occurred thirteen times, or in 35.1 per cent.

In the series of twenty-one cases under consideration all but three of the subjects presented definite signs of aortic insufficiency during life. In one case, a man who died shortly after admission to the hospital from epidemic meningitis, no cardiac murmurs were heard, and in two other instances only apical systolic murmurs were noted at the physical examination. Most of the individuals were middle-aged or young. In 17 cases In 11 cases, or a little over half the number, there was a definite history of syphilis or syphilitic lesions (gummata) were discovered at autopsy. In the remaining 10 cases the possible occurrence of syphilis was not noted in the history.

Although a history of rheumatic fever was obtained in a few instances, it was, on the whole, rather conspicuous by its absence. In 8 cases it was stated positively that the patient had not had rheumatism; in 3 cases there had been "rheumatic pains," and in 3 cases there was a definite history of rheumatic fever. In 6 cases the history was not taken with sufficient accuracy to determine whether or not the patients had had rheumatism.

To determine the relative importance of the association of mesaortitis with aortic insufficiency it was necessary to compare these twenty-one cases with all the other cases of chronic aortic endocarditis, and particularly with those cases which were associated with endarteritis deformans and calcification of the aorta.

Including the above group, 76 cases of chronic aortic endocarditis were found in the 930 autopsies.

In twenty-one of these cases the aortic valves were affected in combination with the mitral or tricuspid valves, and frequently an aortic insufficiency was combined with mitral stenosis or mitral insufficiency. In most of these 21 cases the disease occurred in young people and in a large proportion the disease could almost certainly be ascribed to rheumatic fever. Since this

group of cases in which there are combined lesions of the mitral, aortic and often tricuspid valves is perfectly familiar, the subject needs no further discussion. Suffice it to say that the aorta in every instance was smooth and delicate in appearance, so that the possibility that a sclerosis might have had some effect in bringing about the lesion of the aortic valve is effectually excluded.

In the remaining thirty-four cases of chronic aortic endocarditis in which there was no mesaortitis, the aortic valves alone were affected and showed changes varying from a moderate thickening to a marked thickening, stiffening and calcification. In all but nine of the cases there was sclerosis of the root of the aorta, consisting of patches of yellow thickening of the intima which often showed degenerative change and calcification. Frequently the calcification was very well marked. The lesions were not confined to the root of the aorta, but often were much more advanced in the thoracic and especially the abdominal portion. In most instances the patients were elderly individuals; twenty-two, or 66.6 per cent., were over 50, and twenty-eight were over 40 years of age. In one instance the age of the patient was not given.

The condition noted in this group of cases is so familiar and is found so frequently in autopsies on old men and women that it needs scarcely any comment. Clifford Albutt,[10] contrary to the opinion which is often expressed, has stated that aortic insufficiency is not essentially a disease of old age and that it is of rather exceptional occurrence in the decay of life. The present records are in accord with this view, for in only four of the thirty-four cases, or 11.9 per cent., were there signs of aortic insufficiency during life. In two of these cases there was calcification of the aorta. One of the cases, which occurred in a man aged 46 who had had syphilis, has been placed in this group, though the exact type of

10. Allbutt, Clifford: System of Medicine, Diseases of the Aortic Valves.

sclerosis of the aorta is doubtful, owing to the fact that no tissue was preserved for microscopic study. The aorta showed areas of calcification, which is so unusual in mesaortitis that, without more definite knowledge, the case cannot be considered as belonging to the cases of mesaortitis. In one other case no cardiac murmurs were heard during life, the patient lived but a short time after admission to the hospital, but at autopsy there was found a markedly dilated heart and rather extensive thickening of the aortic valves. The aorta showed advanced calcification. From the extent of the aortic lesion it seemed very probable that if the heart had been examined before the break in compensation the murmurs of aortic insufficiency might have been present.

As might have been supposed, however, systolic murmurs, heard with varying intensity either at the apex or base of the heart, were common in this group and occurred in thirteen cases. It will thus be seen that, while thickening, stiffening and calcification of the aortic valves frequently goes hand in hand with calcification of the aorta and endarteritis deformans, these changes seldom gave rise to true aortic insufficiency.

In the accompanying table the cases of chronic aortic endocarditis are tabulated and show definitely the comparative frequency of the combination of aortic insufficiency and mesaortitis.

AORTIC INSUFFICIENCY AND MESAORTITIS

	Mesaortitis (Pure Aortic Endocarditis).	Endarteritis Deformans (Pure Aortic Endocarditis).	Rheumatic Fever, Etc. (Combined Aortic Endocarditis).
Aortic insufficiency	18	4	21
Chronic aortic endocarditis without signs of aortic insufficiency	3	30	00
Total	21	34	21

It may thus be seen that of the 43 cases of true aortic insufficiency giving symptoms, 18, or 41.8 per cent., were associated with mesaortitis, and of the 22 cases of aortic

insufficiency uncombined with lesions of any of the other valves 18, or 81.5 per cent., were associated with mesaortitis.

It is a matter of common knowledge that syphilis is an important factor in the etiology of aortic insufficiency, but until recent years it has been difficult to prove this matter satisfactorily and to determine in exactly what proportion of cases the condition could be ascribed to syphilis. Siehe and Saathoff[11] have recently called attention again to the frequent association of syphilis and aortic insufficiency. In 7 cases of aortitis luetica which they report aortic insufficiency was present in 6. Albrecht[12] believed, too, that syphilis is the most important cause of aortic insufficiency. Citron,[13] investigating this same point, obtained a positive Wassermann reaction in ten out of sixteen cases of aortic insufficiency, or in 62.6 per cent. Investigations on this point are now being made, but at the present time the number of cases studied is too small from which to draw conclusions.

The practical bearing which such findings have on the treatment of these cases of pure aortic insufficiency becomes at once apparent; for, though one cannot hope to cure the aortic lesion, still the process may perhaps be arrested and the progress of the disease of the aorta influenced by the vigorous use of antisyphilitic treatment.

SUMMARY

In these statistics it may be seen that aortic insufficiency unassociated with disease of the other valves is rare after the fifth decade, and that it is seldom associated with that type of arteriosclerosis known as endarteritis deformans. The majority of cases of uncomplicated aortic insufficiency (81.5 per cent. in the present series) are associated with a characteristic type of sclero-

11. Siehe and Saathoff: München. med. Wchnschr., 1906, liii, 2050.
12. Albrecht: München. Med. Wchnschr., 1906, liii, 332.
13. Citron: Berl. klin. Wchnschr., 1908, xl, 2142.

sis termed mesaortitis. The involvement of the valves takes place probably by direct extension of the process along the wall of the aorta to the aortic valves. Syphilis is certainly the commonest cause of this type of sclerosis.[14]

342 South Fifteenth Street.

ABSTRACT OF DISCUSSION

DR. RICHARD C. CABOT, Boston: Since Dr. J. H. Wright called attention to the presence of spirochetes in the aorta of five cases of heart disease postmortem, we have been able to identify during life some cases similar to those to which Dr. Longcope has called attention. Some patients with heart disease, particularly of aortic disease, without a history of rheumatic or pyogenic infection, but with a history of syphilis and a positive Wassermann reaction in the blood, do respond to antisyphilitic treatment better I think than one would expect such patients to respond to the ordinary type of treatment with rest, digitalis, purgation and cardiac stimulation. In other words, in cases which we believe to be the result of syphilitic infection, pushing the iodids and mercury gives better results than could be obtained under the ordinary treatment. This is a point of great practical value. We should push antisyphilitic treatment in all these cases of non-rheumatic cardiac disease in which there is a history of syphilitic infection, especially if the Wassermann reaction is obtained.

DR. ALLEN A. JONES, Buffalo, N. Y.: In the clinical history of these cases, was there any record of chest pain or anginal pain? In a recent case I studied, a man of 46 had syphilis and shortly before death he gave a positive Wassermann reaction, but there was no history of aortic insufficiency. He had two severe attacks of angina pectoris and died during the third attack.

DR. WARFIELD T. LONGCOPE, Philadelphia: The point made by Dr. Cabot is an important one and the probability is that many of these patients would be much benefited by antisyphilitic treatment. The patient whose case I reported had severe substernal pain and one or two definite attacks of angina. That, of course, is common in this type of cases on account of the involvement of the coronary arteries.

14. Since the completion of this work Collins and Sachs have reported the results of their study of the Wassermann reaction in cardiovascular disease. In 12 out of 13 cases of aortic insufficiency they obtained a positive reaction. In contrast to these findings only 1 of the 7 cases of diffuse endocarditis affecting the mitral valve gave a positive result. They point to the importance of syphilis as a cause of aortitis insufficiency and emphasize the value of antisyphilitic treatment in such cases.

THE VALUE OF ALIMENTARY LEVULOSURIA IN THE DIAGNOSIS OF HEPATIC CIRRHOSIS *

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Any condition bringing about macroscopic or microscopic changes in an organ must of a necessity be accompanied by disorders of the normal function of that organ. On the other hand, there are some functional disturbances of the body and its organs, collectively and individually, which so far as we know are unaccompanied by any microscopic or macroscopic alterations of structure. Investigators interested in this particular field are devoting more and more attention to the functional consequence of organic disease. We are not content now simply to make a clinical diagnosis of a condition, but we demand to know what physiologic change is brought about by the morbid process we are studying. When it is recalled to what extent the literature has been enriched by the reports of investigators, in regard to testing the function of various organs, the publications pertaining to methods for determining disturbed hepatic function seem insignificant. The nervous and cardiovascular systems have been systematically studied; the lungs have received some attention; the stomach, the intestines and the kidneys are claiming their quota of experimental and clinical work, and functional tests for all are described, confirmed and constantly used by the

* From the private laboratory of Dr. John H. Musser.

foremost clinicians. Yet, despite the inestimable advantages which we have derived from some of these tests, we seem to know of none we can call to our assistance to aid us in diagnosing cases of functional disturbances of the liver.

Investigators there have been who claimed to have found clinical tests for such conditions, but one by one these have fallen into oblivion for want of confirmation. The following may be cited as illustrations:

The toxicity of the urine was thought by Bouchard[1] to be an indication of hepatic insufficiency. Schapiro,[2] in studying the question of prognosis in liver cirrhosis, stated that he found a more rapid output of strychnin, given in medicinal doses, in liver cirrhosis than normally. He also states that he found glycosuria followed 200 to 250 gm. of sugar given in the form of fruit preserves to cirrhotics, a fact which he did not properly interpret, and to which I shall refer again. Schwarz[3] eight years later, made some experiments based on Minkowski's observations that after liver extirpation lactic acid appeared in the urine. He gave 15 gm. sodium-lactate and determined the time of the appearance and the amount of lactic acid. Schwarz found that cirrohsis and functional disturbances did not affect the output, but that the lactic acid appeared later than normally, and concludes that it may be explained on mechanical rather than on chemical grounds.

The most marked advance on our knowledge of the subject we owe to Strauss,[4] who approached the question from three points of view:

1. Detoxicating process.
2. Protein metabolism.
3. Carbohydrate metabolism.

1. *Detoxicating Process.*—He observed an increase of fatty acids in the urine of cirrhotic patients. Munk

1. Bouchard: Quoted by Strauss, Deutsch. med. Wchnschr., 1901, pp. 757 and 786.
2. Schapiro: St. Petersburg. med. Wchnschr., 1891, p. 241.
3. Schwarz: Wien. med. Wchnschr., 1899, p. 1754.
4. Strauss: Deutsch. med. Wchnschr., 1901, p. 757.

some time before had found that the toxicity of a soap solution was two and one-half to three times as great when it was injected into the great body veins as it would be if it were injected into the portal veins, owing to the detoxicating action of the liver. Based on this report, Strauss gave 20 gm. sodium butyrate in 8 cases: 5 cirrhosis, 2 carcinoma and 1 chronic obstruction of the common duct. In 6 cases he found increase of fatty acids, in 1 of carcimona and in 1 of obstruction, no increase; but he lays no importance on this, as the same was observed in fever, lead-poisoning and diabetes. He regards the test as valueless.

2. *Protein Metabolism.*—With protein metabolism he had no definite results, and he believes that the study of the relation of urea to total nitrogen is worthless as a test.

3. *Carbohydrate Metabolism.*—This part of his study was based on the research of Sachs,[5] who, working under Strauss' direction, found that in frogs, after extirpation of the liver, there was a lessened tolerance for levulose, but not for dextrose, galactose and arabinose. Sachs made some clinical experiments and found that healthy individuals, as well as diabetics, stood levulose better than dextrose, whereas in liver diseases the tolerance to the same amount of levulose was very much diminished. In a later paper Sachs[6] showed that only the liver was able to form glycogen from levulose, the muscles having no such property, so that it was fair to assume that alteration in hepatic function would be expressed in a diminished tolerance for levulose.

Strauss followed up this very broad hint in 87 cases, 58 of the subjects being healthy as to their liver, clinically, and 29 hepatic cases. Of the latter, 26, or 90 per cent., showed levulosuria, while of the healthy subjects 6 showed levulosuria, giving a percentage of 10. Strauss thinks that this 10 per cent. error—one might call it—

5. Sachs: Ztschr. f. klin. Med., 1899, 38, p. 87.
6. Sachs: Ztschr. f. klin. Med., 1900, 41, p. 434.

may possibly be no error, as there was no way of knowing, apart from clinical study, whether there was any latent disease of the liver or not. In fact, 2 subjects were drunkards, and suffering from obesity and gout; 1 had pneumonia (Rosenberger[7] found levulosuria to occur quite frequently in this condition) showed chronic fever, 1 anemia from gastric hemorrhage, and 1 had some hepatic congestion secondary to mitral stenosis.

In the cases of liver disease not showing levulosuria 1 was atrophic cirrhosis with severe diarrhea interfering with absorption of levulose; the second was acute cholecystitis of two days' duration; and the third was a cyst of the liver.

Furthermore, Strauss found two cases of diabetes showing levulosuria, which is remarkable, as ordinarily diabetics excreted more dextrose after levulose ingestion.

Unlike most observers advancing a new idea, Strauss says that not too much weight should be placed on the test alone, but that a final diagnosis should be made only after careful weighing of the data derived from clinical and laboratory examinations. He made eight observations with 150 gm. cane-sugar and found once glycosuria, four times levulosuria, once saccharosuria and two negative.

In 20 liver cases he found alimentary dextrosuria but once, which is in marked contrast to the French observers, who found it quite a usual occurrence. This discrepancy is best explained by the fact that these men used cane-sugar as a test instead of dextrose (see Schapiro[2]). DeHaan[8], in fact, reported 29 cases studied with regard to the assimilation of glucose and found 18 positive and 11 negative, but his own statement of having used 150 gm. of cane-sugar, and only in doubtful cases having recourse to the polariscope, robs his paper of any

7. Rosenberger: Deutsch. med. Wchnschr., 1906, p. 994.
8. De Haan: Arch. f. Verdauungskr., 1898, iv, 4.

scientific value. Lépine[9] shares this view, and in his article he contributes one case of liver disease showing alimentary levulosuria.

Bruining[10] studied 21 hepatic cases with levulose, saccharose and glucose. Of the 12 cases studied with levulose, he found 10 (all cirrhosis) positive and 2 negative. Of these two, one was carcinoma of the stomach and liver, with absence of free hydrochloric acid and much lactic acid, which he thinks interfered with absorption of levulose; the other case was one of cirrhosis. Here, then, in 11 cases of cirrhosis he found 10 positive with levulose, or 90 per cent., corresponding exactly with Strauss' figures; and Bruining lays great stress on the importance of this test. With saccharose, it might be stated, he got 13 positive glucose reactions. He hints at the future possibility of diagnosing liver diseases by the way various sugars are utilized, and reports cases, one beginning cirrhosis, one of catarrhal icterus, and one in which there was no alimentary glycosuria or levulosuria, but after saccharose there appeared glycosuria in all three. He does not explain this apparently strange phenomenon.

Baylac and Arnaud[11] in the same year at the French medical congress, held in Toulouse, made a report on the clinical value of alimentary levulosuria, based on the study of 23 liver cases. Of these 21 showed levulosuria, or a percentage of 91 positive reactions. Of 20 cases presenting no symptoms referable to the liver, they found alimentary glycosuria in 7, or a percentage of 35, which is in marked contrast to the 10 per cent. of Strauss. Baylac and Arnaud guardedly add, that as these apparently liver-healthy cases occurred in hospital patients, it may be that there was some derangement of hepatic function, which would account for some of the reactions.

9. Lépine: Semaine méd., 1901, p. 105.
10. Bruining: Berl. klin. Wchnschr., 1902, No. 25.
11. Baylac and Arnaud: Compt. rend. Congr. franç. de. méd. Toulouse, 1902, ii, 98.

Landsberg[12] the next year gives his experience with 21 cases of liver disease, only 9 of which or 43 per cent. gave a positive result.

TABLE 1.—LEVULOSURIA IN 21 HEPATIC CASES (LANDSBERG)

Disease.	No. cases.	Pos.
Carcinoma	4	1
Cirrhosis	11	4
Hypertrophic cirrhosis	2	2
Congested liver	1	0
Icterus after calculi	1	0
Chronic obstruction of common bile-duct	2	2
	21	9

To prove his point regarding the futility of levulose as a test, he gave levulose to seven healthy persons. He obtained positive results in four, and concluded that Strauss probably took far-advanced cases for his series, in which a collateral circulation had been established, and that in this way there was rapid entrance of levulose into the blood and urine. On these seven cases he makes the rather bold assertion that as the test is positive in health, it has no value clinically, adding that he believes idiosyncrasy plays more of a rôle in alimentary levulosuria than does functional disease of the liver.

Although hardly bearing on this subject, an observation of Samberger[13] has some significance. Briefly stated, Samberger endeavored to prove that the urobilinuria seen so often in syphilis was of hepatic origin, and selected as his vehicle levulose as recommended by Strauss, with results in accordance with Strauss, Sachs Bruining and others, i. e., urobilin was present in those cases which showed levulosuria.

In 1904 Chajes[14] collected all reports on alimentary levulosuria published up to that time, adding 21 normal cases, showing only one positive levulose reaction. He includes in his table 16 cases published by Ferannini with 11 positive reactions or 69 per cent. Of 84 reported cases of clinically diseased livers, Chajes found 86 per cent. showing alimentary levulosuria; of 99 sound

12. Landsberg: Deutsch. med. Wchnschr., 1903, p. 563.
13. Samberger: Arch. f. Dermatol. u. Syph., 1903, p. 89.
14. Chajes: Deutsch. med. Wchnschr., 1904, p. 696.

as to their liver, 15 per cent. showing alimentary levulosuria. He concludes the former is about the percentage of alimentary levulosuria.

Von Halász[15] criticizes Strauss' work, as he thinks that the patient might have had a low assimilation limit for all sugars, but he confirms Strauss' observations and those of other writers. Von Halász thinks the test of great service in deciding between cirrhosis and other conditions, and states that normally 100 gm. levulose rarely causes levulosuria; a positive result therefore speaks for the presence of a diffuse and consequently severe disease of the liver, especially indicative of cirrhosis.

The method of examination adopted in this series was as follows: No food was given the patient after the evening meal. The patient voided his urine at a stated hour the next morning, after which, on a fasting stomach, he was given 100 gm. of levulose dissolved in 500 c.c. tea or water according to taste, the whole amount being taken within fifteen minutes. At the termination of each hour thereafter, for four consecutive hours, the urine was collected in four separate bottles, after which breakfast was eaten. It was impossible in some instances to obtain urine each hour, in which case collections every two hours had to be resorted to. Each specimen of urine, including that passed before the beginning of the test, was examined separately by the Fehling, Nylander, Seliwanoff, and fermentation tests, and the combined urine with the exception of the urine before the ingestion of levulose, by the above tests, and in addition by Rosin's method and by the polariscope. As the number of cases increased the spectroscopic examination was omitted. Despite the criticism lately directed against the Seliwanoff reaction by Borchardt,[16] I regard the test as a very useful one, and so far in my experience the disturbing factors mentioned by

15. Von Halász: Wien. klin. Wchnschr., 1908, p. 37.
16. Borchardt: Ztschr. f. phys. Chem., 1908, p. 241.

him have not been met with. Reliance was not placed on this reaction alone, and the presence of levulosuria was accepted as certain, only when there was reduction of the Fehling's and Nylander solutions, fermentation with yeast, a positive Seliwanoff test, and left rotation with the polariscope.

In performing the Seliwanoff test care must be taken not to confuse the rose tint obtained with many urines by boiling with hydrochloric acid, with the typical color reaction due to levulose. In the first instance the shade of red is very light, and fades away entirely on standing or on cooling, while the color in the latter case is a dark magenta red, clouding the entire specimen of urine and deepening on standing or on rapid cooling. The color due to levulose persists for days and there is deposited on the bottom of the test-tube a dark red precipitate.

The cases reported in this paper number thirty-two, and most were seen in the private practice of my chief, Dr. Musser, and in his wards at the University and Presbyterian hospitals. Additional cases were furnished me by Dr. Alfred Stengel, Dr. James Tyson, Dr. D. F. Woods, Dr. E. J. G. Beardsley, Dr. J. H. Musser, Jr., Dr. W. Taylor Cummins, and Dr. M. Solis-Cohen, to all of whom I wish to acknowledge my great indebtedness.

In the first ten cases the tolerance for glucose and saccharose in addition to levulose was tested, but this necessitated so much inconvenience on the part of the patients that it was omitted in the remaining twenty-two cases. I believe, nevertheless, that in all instances in which alimentary levulosuria can be demonstrated, the tolerance for glucose and saccharose should be determined, since there may be, in certain individuals, a normally low assimilation limit for all sugars.

In hepatic disease, after 100 gm. of levulose, the sugar usually appears in the second-hour specimen, after which time it either varies in degree or is absent entirely from the succeeding portions of urine. Strauss has already

observed this phenomenon. The appearance of levulose is tardy and of short duration in cases in which the liver is but moderately affected; it is, however, rapid, intense and prolonged in cases of profound alteration, so that alimentary levulosuria may perhaps be regarded as an early symptom of hepatic disease (cf. Baylac and Arnaud[11]).

I was unable in the majority of instances to confirm the diagnosis by postmortem examinations, so it was impossible to control the extent of the hepatic lesion, but judging from the clinical course of the individual cases, I believe the inference to be drawn from the early or late appearance of levulosuria, as stated above, is correct.

As will be seen from a study of the table, all of the cirrhosis patients exhibited alimentary levulosuria, the early appearance coinciding with severe disorders and the tardy appearance with the clinically mild affections.

One case (No. 3) of marked fatty degeneration (autopsy) showed levulosuria in the first hour.

All of the six subjects of hepatic enlargement due to chronic passive congestion assimilated 100 gm. of levulose easily. In these cases the tolerance was of considerable assistance in arriving at a proper diagnosis.

One patient with ovarian cyst (No. 26; operation) had certain symptoms of cirrhosis, but showed no alimentary levulosuria, and at operation the liver was found to be apparently healthy.

Levulose was given by mistake to the diabetic patient (No. 22) instead of to another patient in the same ward. There was a marked intolerance, which is the more remarkable as diabetics are supposed to utilize levulose well (Külz,[17] etc.).

Alimentary levulosuria was present in one case (No. 27) of catarrhal cholangitis in which a cirrhosis could not be excluded.

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17. Külz: Quoted by von Noorden, Handbuch der Pathologie des Stoffwechsels, 1907, II, 53.

TABLE 2.—LEVULOSURIA IN 32 PATIENTS

(100 Gm. Sugar Administered in Each Case)

Cases.	Form of Sugar.	Excretion by hours 1	2	3	4	Diagnosis.
1	Levulose	—	0	++	+	Cirrhosis
	Glucose	0	+	++	0	
	Saccharose ..	0	0	0	0	
2	Levulose	+	+	0	0	Cirrhosis
	Glucose	0	0	0	0	
	Saccharose ..	0	0	+	+	(levulose test)
3	Levulose	+	++	0	0	Fatty degeneration
	Glucose	0	0	0	0	
	Saccharose ..	0	0	0	0	
4	Levulose	0	+	+	—	Cirrhosis
	Glucose	0	0	0	0	
	Saccharose ..	0	0	0	0	
5	Levulose	0	++	+++	+	Cirrhosis
	Glucose	0	0	0	0	
	Saccharose ..	0	0	0	0	
6	Levulose	+	++	+	+	Cirrhosis
7	Levulose	+	+	+	+	Cirrhosis
8	Levulose	—	0	0	+	Cirrhosis
9	Levulose	++	+	+	—	Cirrhosis
10	Levulose	+	0	0	+	Cirrhosis
11	Levulose	+	++	+	+	Cirrhosis
12	Levulose	+	+	++	0	Cirrhosis
13	Levulose	+	++	+	0	Cirrhosis
14	Levulose	+	++	+	0	Cirrhosis
15	Levulose	+	0	+	++	Cirrhosis
16	Levulose	+	+++	+	0	Cirrhosis
17	Levulose	0	+	+	0	Cirrhosis
18	Levulose	—	+	+	+	Cirrhosis
19	Levulose	0	—	+	0	Cirrhosis
20	Levulose	0	+	++	+	Cirrhosis
21	Levulose	+	++	+	+	Cirrhosis
22	Levulose	+	++	+++	+	Diabetes
23	Levulose	0	0	0	0	Myocarditis
	Glucose	0	0	0	0	with secondary hepatic congestion
	Saccharose ..	0	0	0	0	
24	Levulose	0	0	0	0	Tricuspid insuf.
	Glucose	0	0	0	0	with hepatic congestion
25	Levulose	0	0	0	0	Chronic Pass.
	Glucose	0	0	0	0	cong. Myo-
	Saccharose ..	0	0	0	0	carditic Nephritis
26	Levulose	0	0	0	0	Ovarian cyst
	Glucose	0	0	0	0	
	Saccharose ..	0	0	0	0	
27	Levulose	0	++	++	+	Catarrhal Cholangitis. Cirrhosis (?)
28	Levulose	0	0	—	—	Chronic Pass. Cong. Myocarditis
29	Levulose	0	0	0	0	Chronic Pass. Cong. Nephritis
30	Levulose	0	0	0	0	Nephritis. Chr. Pass. Cong.
31	Levulose	0	0	0	0	Syphilitic Cirrhosis (?)
32	Levulose	0	0	+	+	Carcinoma of
	Glucose	0	0	0	0	Gall bladder
	Saccharose ..	0	0	0	0	

SUMMARY

DIAGNOSIS.	TOTAL.	POSITIVE.	NEGATIVE.
Cirrhosis	20	20	0
Cirrhosis (?) Syphilitic	1	0	1
Fatty Degeneration of Liver	1	1	0
Chronic Passive Congestion	6	0	6
Catarrhal Cholangitis-Cirrhosis (?)	1	1	0
Carcinoma of Gall-Bladder	1	1	0
Ovarian Cyst	1	0	1
Diabetes Mellitus	1	1	0
Total	32	24	8

Percentage Positive Reaction 75
Percentage Positive Reaction in Cirrhosis 100
Percentage Positive Reaction in Chronic Passive Congestion .. 0
Percentage Positive Reaction in Disease of Liver, Bile-Ducts and Gall-Bladder 97
Percentage Positive Reaction in Non-Hepatic Disease 12.5

The one patient (No. 31) with supposedly syphilitic cirrhosis utilized levulose perfectly. The clinical diagnosis was at first carcinoma of the liver, but was later changed to the one given in the table.

Patient 32 (carcinoma of the gall-bladder) excreted levulose in the last two hours following ingestion of the same.

CONCLUSIONS

1. Alimentary levulosuria is almost a constant phenomenon in chirrhosis of the liver.

2. The early or late appearance of levulose may be regarded as a sign of severe or mild hepatic disease.

3. Alimentary levulosuria is a useful aid in diagnosing between cirrhosis on the one hand and chronic passive congestion on the other.

4. A study of the hepatic function with glucose and with saccharose in addition to levulose is to be desired, inasmuch as there may be an individual intolerance to carbohydrates.

5. While not indicative of any specific organic lesion of the liver, alimentary levulosuria is most frequently observed in cirrhosis.

248 South Twenty-first Street.

ABSTRACT OF DISCUSSION

DR. DE LANCEY ROCHESTER, Buffalo: Did Dr. Goodman find the reaction positive in cases of mixed cirrhosis and passive congestion?

DR. J. R. WILLIAMS, Rochester, N. Y.: I have attempted to examine some cases in the way described by Dr. Goodman, with unsatisfactory results. Investigations of this sort may easily be carried on in an endowed hospital, but sometimes they are not practicable in private practice. For example, levulose costs about 80 cents an ounce, making the cost of a single examination about $2.50, obviously a prohibitive cost to the general practitioner. I have attempted to carry out the test using honey instead of levulose; honey contains approximately 50 per cent. of levulose. My experience with it is too limited, however, to enable me to express an opinion as to its value.

DR. EDWARD H. GOODMAN, Philadelphia: It was impossible in my series of cases to control the clinical diagnosis by autopsy, so I can not say just how extensive the hepatic lesion was. I obtained levulose from Schering & Glatz of New York, one pound costing $1.60.

INDICANURIA AND ITS SIGNIFICANCE

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Indicanuria is the presence in the urine of a perceptible quantity, more than a mere trace, of the indoxyl sulphate of potassium, of which the chemical formula is $C_8H_6NKSO_4$. It is derived from anaerobic bacterial putrefaction of proteids.

Indol is first produced, and, at the time of absorption, is converted into a soluble indoxyl, which, in the juices of the body, unites with a base, usually potassium, and is excreted in the urine as indoxyl sulphate of potassium. Normally, from 5 mg. to 20 mg. of this substance are excreted daily; abnormally, from 50 mg. to 150 mg.

Numerous tests, most of which I have examined, have been offered for the determination of the presence of indican. The solution of the neutral or basic subacetate of lead, commonly employed to clear the urine, is not without disadvantage. Sometimes it removes a portion of the indican; occasionally it renders the detection easy. As an oxidizing agent a 1 per cent. solution of potassium chlorate is to be preferred to the solution of chlorinated soda, because of the instability of the latter.

The test for indican which is advised is as follows:

To 10 c.c. of filtered urine add one drop of a 1 per cent. solution of potassium chlorate; then add 5 c.c. of chloroform, and lastly 10 c.c. of pure hydrochloric acid of a specific gravity of 1.19. Thorough mixing is obtained by repeatedly and slowly pouring from one test-tube to another. The indigo thus set free is dissolved in

the chloroform, to which is imparted a blue color. The maximum coloration is secured in ten minutes. When large amounts of indican are present, more potassium chlorate will be required.

Clinically, a quantitative idea of the amount of indican present may be obtained by noting the depth of the blue color of the chloroform. Salkowski, Strauss and others have devised methods by which the quantity of indican may be estimated, but most clinicians employ the qualitative method. The presence of a faint bluish discoloration of the chloroform may be viewed as normal or as possessing no importance. If the urine contains iodid the chloroform will be colored violet, which color may be removed by adding three drops of a 5 per cent. solution of sodium thiosulphate. Certain observers have noted that indican is usually absent in normal children under five years of age. Indican may be constantly present in large, moderate or small quantities, or only occasionally present during certain hours of the day or certain days of the week or month. In order, therefore, that the presence of indicanuria be not overlooked it is necessary to obtain urine for examination at different times during the day or week, or under conditions produced by variations in food, exercise, or during the presence of one of the most marked symptoms of this affection, as for example, headache. Indican is often detected in the urine passed after supper (care being taken to instruct the patient to empty the bladder before beginning the meal) and may be absent at all other times. Occasionally it may be necessary to modify the articles of food composing the supper, so as to make it a test meal. The urine first passed on arising and retiring, as well as that taken from a twenty-four-hour specimen, should always be examined. Sometimes indican is observed only after the ingestion of certain articles of food, or combinations of food, which may be indigestible, unsuitable or in excess. It must always be remembered that, owing to an idiosyncrasy, certain patients suffer

acute indigestion with marked toxic symptoms, when they partake of certain foods or combination of foods which may for others be digestible.

Clinically, indicanuria may be mild or severe, acute, chronic, or recurrent, and occurs as an independent affection or as a complication of other diseases. The severe forms of intestinal toxemia simulate cholera and may cause death in less than one week.

Indicanuria is significant of the absorption of the products of putrefaction, which putrefactive material is usually situated in the gastrointestinal tract, but under exceptional circumstances may be in other parts of the body. It is well known that during putrefaction, phenol, cresol, fatty acids and gases, and other substances are elaborated, in addition to indol, skatol or methyl indol. The test for indican is so simple and the test for other putrefactive products so difficult that gradually indican has assumed the position of an indicator of the absorption, not only of indoxyl, but in addition any one or any combination of the bodies produced by the decomposition of proteids.

Indicanuria may be absent when proteid decomposition is present if absorption is prevented, and it is conceivable that intestinal toxemia occurs in the absence of indicanuria.

Indol is a volatile aromatic substance of fecal odor, crystallizing in white glancing crystals, is practically insoluble, and as it passes through the mucous membrane it is converted into soluble indoxyl and is carried by the portal blood to the liver, where it becomes indoxyl sulphate and later the indoxyl sulphate of potassium. When indican appears in the general circulation it is excreted as such by the kidneys.

Jaffé states that the subcutaneous injection of indol is followed by the appearance in the urine of large quantities of conjugated indoxyl compound. Herter maintains that indol is only moderately toxic to man and that small doses may produce frontal headache, mental irrita-

bility, insomnia and mental confusion, and that the continual absorption of enough indol to yield a constant strong reaction of indican in the urine is capable of inducing symptoms of neurasthenia. Skatol is supposed to act as does indol.

Phenol is extremely poisonous, but phenol-sulphate is non-toxic. Phenol is usually coexistent with indican and is increased and decreased in like manner, the principal exception being in anemia and cachexia, in which indican is increased and phenol is decreased, and in hunger, in which phenol is increased and indican is decreased. Cresol is supposed to act as does phenol.

During proteid decomposition of fatty acids, such as formic, acetic and propionic, are formed, and also certain gases, such as carbon dioxid, hydrogen, marsh gas and sulphuretted hydrogen. These acids are probably but moderately toxic in the quantities in which they exist under ordinary conditions; but it must not be forgotten that small quantities of sulphuretted hydrogen are extremely poisonous. On one occasion I administered per rectum sulphuretted hydrogen, which produced simultaneously rapid, intermittent, weak pulse, collapse, delirium, and a slight odor of this gas in the breath. These symptoms vanished in a few moments.

It is not improbable that in certain cases unknown or undiscoverable toxalbumins are formed which may be peculiarly poisonous even in very small quantities. No exact knowledge exists as to the precise manner in which the body protects itself from the poisonous compounds produced during proteid decomposition, but it is believed that such an influence is exerted by the cells of the liver and intestinal mucous membrane. Baumann was able to demonstrate that the liver contains a larger amount of ethereal sulphates than does the blood. Clinically, indicanuria occurs more readily when the hepatic function is disturbed than when this organ is normal. Indicanuria not infrequently exists without symptoms. Occasionally putrefactive bodies are produced that are but slightly

toxic, and certain individuals possess an inherited or acquired immunity, while others are peculiarly susceptible to very small quantities of these bodies. As it is unsafe to assume, in the light of our present knowledge, that indicanuria produces no harm when symptoms are absent, prudence dictates the prevention of its formation.

The conditions which favor indicanuria are numerous and demand attention. Morbid conditions of the teeth, mouth, oropharynx, nose and sinuses connected therewith, in their relation to the production of indol, possess an importance which is far too little recognized. Not infrequently the buccal cavity contains much decomposing material, together with many micro-organisms, both fermentative and putrefactive. The odor often suggests decomposition and examination may reveal abscess of the gums, pyorrhea alveolaris, with soft, flabby, congested and contracted gums, forming numerous cavities, in which pus and food may be retained under conditions peculiarly favorable to decomposition. A similar condition may arise from the long-continued presence of food between the teeth, especially when there is irregular dentition or caries. Occasionally in the enlarged crypts of diseased tonsils decomposing cheesy material may be found and suppurative rhinitis or sinusitis is not uncommon. When such conditions of the oropharynx, nose or sinuses exist it is manifest that food, even during mastication and before deglutition, may become infected and putrefaction begin.

Many causes favor the production of indol, such as simple excess of proteids from gormandizing; insufficient mastication or insalivation and too rapid eating; any condition paralyzing or lessening gastric, intestinal or colonic peristalsis, or retarding the onward progress of the gastrointestinal contents or interfering with the normal secretions of the stomach, intestines, pancreas or liver, etc. It is evident, therefore, that indicanuria is to be expected in gastrointestinal or colonic atony or paral-

ysis as well as in relaxation of the abdominal wall, producing gastroptosis or enteroptosis. Again, hernia, ileus, appendicitis, local or general, acute or chronic peritonitis and pyloric or intestinal stenosis, constitute conditions favoring the growth of putrefactive bacteria.

The absence, diminution or excess of hydrochloric acid, by producing indigestion and fermentation, favor the production of indol.

Indicanuria has been observed in diarrhea, in association with indigestion, gastritis, enteritis, colitis, ulceration or obstruction of the small or large intestines, cholera, dysentery, Addison's disease and inanition. The deep importance of the recognition of indicanuria as a complication in typhoid fever I emphasized in 1904, in a communication read before the Pennsylvania State Medical Society.

Constipation may exist without indicanuria, but is exceptional. Normal feces, the product of normal digestion in a normal individual, may remain in the colon an undue length of time without toxicity. Acute attacks of indigestion with furred tongue, offensive breath, constipation, mental and physical depression and headache, familiarly known as "biliousness" or congestion of the liver, are usually associated with indicanuria, and, in many instances, are examples of acute toxemia due to absorption of products of decomposition of the intestinal contents. It is more than probable that minor attacks of toxicity occur without well-marked symptoms. Recurring attacks of simple hepatic congestion, due to toxic poisoning, interfere with the normal excretion of bile, which in turn incites intestinal indigestion, fermentation and putrefaction, thus preparing the way for a similar attack on slighter provocation. In the course of months a chronic congestion of the liver is produced, aggravated by recurrent attacks of acute congestion, and thus, if the toxemia be moderate, in the course of years the clinical picture of hepatic cirrhosis may be developed.

Excessive formation of indol has been observed in various morbid states of the liver, with or without jaundice, in diseases of the pancreas, as well as in suppurative and gangrenous conditions of other parts of the body, as, for example, in empyema, gangrene or abscess of the lung and perityphlitic abscess; and has also been observed after the administration of turpentine or creosote.

Having thus far treated of indican as an indicator of toxemia, let us now turn to the various effects of toxemia.

Acute attacks of toxemia are frequently associated with dark-colored urine showing hyperacidity, high specific gravity, indicanuria and skatoluria, or moderate albuminuria and choluria, cylindroids and a few hyaline tube casts. As the toxemia increases in frequency and intensity, or becomes chronic with exacerbations, the albuminuria and cylindruria increase, and eventually, in consequence of long-continued irritation of the kidneys produced by the excretion of chemical irritants, resulting from intestinal putrefaction, chronic interstitial and parenchymatous nephritis develop. In the early stages, under appropriate treatment, these abnormal constituents in the urine disappear; again, in moderately severe cases, three, four or five years may elapse before this result is obtained.

The circulation in the blood of the derivatives of putrefaction absorbed from the intestines produces varying degrees of anemia, which, as a rule, is of the chlorotic type, and in long-standing and severe cases this anemia may become so extreme as closely to simulate the clinical and blood picture of pernicious anemia. The poison causes a rapid loss of hemoglobin and a slow loss of erythrocytes, but does not materially interfere with the leucocytes.

The circulation in the blood of these toxic substances at irregular intervals over a period of many years may cause the development of arteriosclerosis from direct action on the walls of the vessels. In a number of cases

the conclusion was irresistible that this was the cause of arteriosclerosis.

The relationship of indicanuria to the nervous system is varied and most interesting. Several cases of neuro-retinitis, associated with persistent and marked indicanuria, have gradually subsided and then disappeared, when this chronic poisoning was prevented; and in like manner, neuralgia or inflammation of other nerves have been produced. Occasionally pains in various parts of the body, due to intestinal toxemia, have been erroneously ascribed to rheumatism or gout. One of the common symptoms of acute or chronic intestinal toxemia is headache, either mild or severe, usually frontal, although it may be in the vertex or occiput. The duration varies from a few hours to a few days and may occur at intervals of two or three days, or as many weeks or months. An intermittent headache from this cause may continue unrecognized for months, and in one instance has been endured for seventeen years. Intestinal toxemia is as frequent a cause of headache as errors of refraction. Several examples of persistent insomnia, chiefly due to putrefactive poisoning, have come under my observation during the past decade. Certain individuals are peculiarly susceptible to minute quantities of putrefactive poison; this peculiarity has been especially observed among neurasthenics, in this respect resembling the well-known idiosyncrasy to alkaloids, such as atropin, etc. Chronic intestinal toxemia may induce or complicate cases of neurasthenia. It is not improbable that one of the reasons for the favorable results obtained from the use of a milk diet in treatment of neurasthenia is the incidental removal of an unrecognized toxemia.

Again, intestinal toxemia is a common complication of the various forms of mental diseases as seen at the Philadelphia Hospital, and occasionally it is the cause or complication of certain cases of epileptiform convulsions. The favorable course of many cases of pulmonary tuberculosis is interrupted by attacks of intestinal tox-

emia, and has been more frequently observed since the treatment of tuberculosis by large quantities of milk and eggs has become more general. The diagnosis of this complication is absolutely necessary for success in treatment of tuberculosis where a specific diet, suitable for the individual, should be substituted for the one in more general use. Putrefactive poisoning aggravates catarrhal inflammations of the respiratory tract and the recognition and removal of this complication is frequently followed by a marked amelioration of symptoms, and in like manner certain cases of bronchial asthma are greatly benefited. Eczema, pruritus, acne rosacea, and malodorous perspiration and breath have been observed in association with indicanuria.

Intestinal toxemia is a common disease in itself and a frequent complication of many diseases; its removal is very frequently followed by remarkable and prompt amelioration or disappearance of many distressing symptoms.

317 South Eighteenth Street.

ABSTRACT OF DISCUSSION

DR. HEINRICH STERN, New York: The pathologic significance of urinary indican, or rather indoxyl-sulphuric acid, has been grossly exaggerated. True, there ensues an increased production of indoxyl compounds in cholera, Addison's disease, obstructive affections of the small intestines, etc., but this does not justify us in ascribing to them toxic qualities, and to maintain that they stand at the foundation of a number of pathologic conditions. Of course, the indoxyl compounds have no direct relationship to so-called pyorrhea alveolaris, they are neither its cause nor its result. The indoxyl compounds are normal urinary constituents and we find them in small amounts in every human urine, except in that of new-born and breast-fed infants. Indoxyl is even contained in the renal secretion of infants who obtain besides human milk also some cow's milk and even in these instances, it occurs in the absence of any digestive disturbances whatsoever. Increased amounts of indoxyl as found in the urine allow of but one interpretation, namely, that we are confronted with some form of tryptic perversion. Some observers hold that the trypsin of the pancreatic secretion induces or favors the production of indoxyl. Their contention is based on two facts, viz.: the tryptic quality as regards decomposition of the ingested proteid material, and the decrease of

urinary indoxyl in case of an occlusion of the pancreatic duct. Clinical experiments and observations, however, have demonstrated to my satisfaction that in the majority of instances of so-called indicanuria, we have to deal with an insufficiency of tryptic function and, consequently, with abnormal putrefactive processes and the augmentation of the intestinal bacterial flora. While it is, of course, possible that an indicanuria may occur with a process like pyorrhea alveolaris while it is even possible, although it has never been proved, that perverse intestinal putrefaction may stand in some more or less remote relationship to pyorrhea alveolaris, we have no business to maintain that one of the accidental products of such putrefaction, the indoxyl, is the true causative agent of this or of any other affection. We must not forget that pyorrhea alveolaris is an exceedingly progressive, chronic affection, and that indicanuria, that is the excessive excretion of indoxyl compounds, is essentially an acute, or at least, a limited occurrence. Is it possible that the rather ephemeral indicanuria will give occasion to the enduring pyorrhea? The same contention holds good with all other affections which, at one time or another, have been accused of having excessive excretion of indoxyl as their causative factor. The indoxyl compounds are not toxic in themselves, so far as we know, they are of more or less accidental occurrence, and may point to an occlusion of the small intestine with a decrease of tryptic function and an increase of bacterial activity. Everything else belongs to the realm of speculation. Moreover, I wish to direct attention to the fact that indoxyl occurs not only in the urine of carniverous but also in that of herbiverous animals. As a matter of fact, it is present in the urine of some of the herbivora in much larger quantities than in any of the carnivora. It occurrs in enormous amounts in the urine of the horse, from which we obtain it for experimental purposes. It may also be prepared from the urine of the dog, but, in my experience it is purer when it is derived from horse's urine. In the latter, it is present in larger proportion than in that of cattle. The reason for this seems to be the large cecum of the horse which permits additional and more complete disintegration of the ingested material. Indoxyl does not occur in the urine of the rabbit, as a general rule, but I have found it therein in the presence of artificially induced obstipation. While indoxyl appears in the urine in larger amounts after a diet rich in animal food, it never attains pathologically that proportion in the human being which is normally present in the urine of the horse. This evinces, I dare say, that animal food and the ensuing putrefactive processes, in herbivorous animals at least, are not the only source of indoxyl compounds and that vegetable ingesta and fermentative processes may give rise to indican production. I have employed for some time the potassium

chlorate-chloroform-hydrochloric acid test advocated by Dr. Daland for clinical work.

Dr. Henry R. Harbower, Chicago: The subject under discussion appears to be unquestionably the entering wedge to even more important and vital studies. Dr. Daland has rightly emphasized the significance of indicanuria and its importance as an etiologic factor in disease. A point which I wish to emphasize, however, is the close relation between indicanuria and diseases of the mouth and teeth. As a matter of fact, mouth symptoms are among the first manifestations of those disturbances due to or associated with indicanuria and its causes. Acid saliva, pyorrhea and affections of the alveolar process are almost invariably accompanied by indicanuria. The pioneer work in this particular line of Dr. Eugene S. Talbot of Chicago proved this assertion. Acidemia is also frequently found associated with indicanuria; I do not refer to the acidosis of diabetes. In a series of several hundred uranalyses the average acidity was increased considerably, varying from 10° to 275°, the normal degree of acidity being from 30° to 40°. Each degree represents the amount of N/10 sodium hydrate required to neutralize 100 c.c. of urine. The number of acid units (and, by the way, this is an important factor recently suggested by Dr. A. L. Benedict of Buffalo) varied from about 8,000 to 350,000 in twenty-four hours, 40,000 being approximately the normal. In 83 per cent. of these cases indican was present to a greater or less extent, those cases showing an excess of indican always giving a marked increase in acidity. A number of cases showing indigo red instead of indigo blue all evidenced a tremendous acidity. In 81 per cent. of this series the urea index was diminished an average of one-half; in one case in which the acidity reached 220 and indican was abundant the percentage of urea was only 0.4 (2.8 gm. in twenty-four hours). About one-third of these cases showed casts. Summing up these facts it will be seen that indicanuria is practically always associated with an excessive elimination of acid substances in the urine and a marked decrease in the amount of urea, two very important findings. I believe that the condition of acidemia or diminished blood alkalinity is of far greater importance than present medical opinion or the text-books would lead one to believe; that it is a probable cause of many obscure diseases and consequently deserves more extended attention and thorough investigation. Further, the reduction of this condition of excessive acidity by the judicious use of suitable remedies brings with it a speedy and decided amelioration of many indefinable ills.

Dr. Richard C. Cabot, Boston: After using the test for indican for a long time in different clinical conditions, I have given it up and I would advise others to give it up. We

sometimes get an increase of indican in the urine in pathologic conditions, of course; but in such case the nature of the pathologic condition present is much more obviously indicated from the clinical side. Indicanuria gives us no diagnostic or therapeutic indication. What was the relation of indicanuria and indican production to the diseases Dr. Daland mentioned?

Dr. Allen A. Jones, Buffalo: I think that Dr. Daland has mentioned two points in particular that are worthy of our consideration. The first is that normally from 25 to 50 grams of indican are excreted in twenty-four hours; whereas, abnormally from 50 to 150 are excreted. So I believe that it should be routine work to estimate the amount of indican excreted in twenty-four hours. The indican test has been employed in my laboratory for many years, using the qualitative but not the quantitative test. It may be that by using the quantitative test one may arrive at some definie clinical conclusions. So far as the qualitative test is concerned, very little attention is paid to it at the present time in a routine way except in the laboratories. Years ago an attempt was made to associate indicanuria with a definite condition of the stomach, a diminution of the amount of hydrochloric acid in the gastric contents; in my series of 160 cases, I could not prove any definite relation between the amount of secretion of hydrochloric acid and indicanuria, which was found with and without any diminution in the amount of hydrochloric acid in the gastric contents.

So far as can be gained from Dr. Daland's paper, we can come to but one general conclusion, *i. e.*, indicanuria is merely an evidence or symptom of a toxemia, and this toxemia may come from a variety of conditions. It is not associated with any definite pathologic condition in the body, or in other words, any definite disease.

Dr. Anthony Bassler, New York: My experience is confirmatory of Dr. Jones' statement concerning the relationship existing between states of gastric juice secretion and indicanuria. It is generally taught that the regular association with indicanuria is a low state of gastric juice secretion, but this is not always so. A marked indicanuria may exist with excess stomach secretion. Clinically speaking, I do not think that the indicanuric conditions are only produced by hypochlorhydria and anachlorhydria, but believe that the intestinal conditions called indicanuria often cause depression of the secretory apparatus of the stomach, for by the direct treatment of the intestinal condition its effects on the stomach are often mitigated or removed. I regret that Dr. Daland did not have time to describe his test, and I wish he would add whether the use of the solution he advocates will also give the uroresin reaction, which to me is just as important as indican.

DR. JUDSON DALAND, Philadelphia: I think that Dr. Jones' understanding of indicanuria is the correct one, namely that it is simply an indicator of the absorption of putrefactive substances, a certain toxemia. Much benefit is derived from the study of the presence of indican in the urine. To me, at least, it has been of great service. Indicanuria serves to aggravate certain conditions. To show this, I recall two cases of retinitis under the care of a skilled ophthalmologist, who found that the condition was toxic. Indican was present in the urine in large amounts. By successfully treating the indicanuria the patient made a good and rapid recovery from his retinitis. We can always take exceptions to clinical evidences; but clinical evidence is necessary because we are not in a position to offer experimental evidence. I have had the opportunity of watching the renal secretions under many conditions in association with indicanuria, and I have observed its disappearance followed by a clearing up of the evidences which make some believe there is an involvement of the kidney. I desire to repeat that indican itself is not a substance capable of producing any material interference with health; but in those conditions in which there is the continued presence of a large amount of indican I have found associated evidences of disorders of various parts of the body which, in my opinion, were due to the formation in the intestine of toxic substances of different kinds which I am unable to differentiate. Therefore, I use this test as a rough clinical method; when indicanuria is present, by causing the removal of the indican from the urine we improve the patient very materially. This is merely a clinical contribution. I was especially glad to hear Dr. Harrower speak of the condition of acidemia or diminished blood alkalinity.

TROPICAL DISEASES—AMERICA'S OPPORTUNITIES AND OBLIGATIONS

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The race for empire from its beginning has suffered more from disease and pestilence than from the implements of war. This fact has furnished many examples of stimulation to medical research. None is more striking than that given to the study of the diseases of warm climates as a result of the struggle of the nations for the possession of the tropics.

The close of the nineteenth century found the work of the colonizing powers practically at an end, in that nearly all of the available territory of the earth had been entered on and occupied. With these acquisitions, however, the mother countries realized that their work had but begun. To bring these great tracts of earth under the dominion of civilization, to develop their abundant resources, to give peace and prosperity to their fertile soils, they wisely realized that another foe had to be conquered—realized that they must learn the causes, nature, and means of prevention of the diseases which have always formed the greatest barrier to the colonization of these countries.

On August 27, 1897, after ten years of laborious research, under the most disadvantageous circumstances, success crowned the efforts of a hero and scientist—a success which well might inspire his poetic nature to sing:

"This day relenting God
Hath placed within my hand
A wondrous thing; and God
Be praised. At His command

Seeking His secret deeds
With tears and toiling breath
I find thy cunning seeds,
O million-murdering Death.

I know this little thing
A myriad men will save.
O Death, where is thy sting,
Thy victory, O Grave?"

The discovery of Ross that the mosquito is the intermediate host of the malarial parasite, and its confirmation and extension by other distinguished scientists may be said to have stimulated renewed interest in the onslaught on tropical diseases.

With the dawn of the twentieth century we see special institutes established and commissions formed and sent out for the study of these diseases. At the close of the first decade of this work, which has resulted in epoch-making discoveries which vie with those of Jenner and Pasteur; at this meeting, when the American Medical Association is honored by the presidency of Colonel Gorgas, it seems not inappropriate to speak of "Tropical Diseases and America's Opportunities and Obligations" toward the same, notwithstanding the fact that the subject has been dealt with in several excellent addresses recently.

Sir Patrick Manson has pointed out that the "peculiarities of tropical diseases are etiologic rather than pathologic." Passing those conditions, such as insolation, heat-syncope, siriasis and tropical neurasthenia, which are the direct result of climatic and meteorologic influences found in warm countries, certain diseases are encountered which are the result of toxic substances taken in with the food, peculiar to these climates. As example of these may be mentioned ergotism, lathyrism, pellagra, and possibly beriberi.

It has also been customary to include, conventionally, in the list of tropical diseases certain bacterial infec-

tions, such as Malta fever, bubonic plague, leprosy, bacillary dysentery and cholera, because here are found social and hygienic conditions which are conducive to their prevalence. These diseases, however, can flourish in any climate and, therefore, have no real claim to be regarded as strictly tropical diseases.

The most important factor which determines the geographic distribution and limitation of tropical diseases is the fact that "certain pathogenic agents either require high atmospheric temperature for their successful passage from host to host or require an animal intermediary which flourishes only in high temperatures" (Manson). As examples of the former may be mentioned uncinariasis, amebic dysentery and certain parasitic skin diseases; of the latter, malaria, trypanosomiasis, African tick fever, filariasis, yellow fever and possibly dengue.

While this fact of high temperature is found at its best in the tropics, these diseases are by no means confined to the equatorial zone, extending around the earth between the tropics of Cancer and Capricorn. The same condition is found in subtropical regions, and in the temperate zone during the summer season. Our increasing knowledge of these diseases is demonstrating their prevalence in these regions.

So keen has been the interest; so great have been the achievements in tropical diseases during the last decade, that it will manifestly be impossible for me to do more at this time than to call attention to some of the more important advances which have been made in this domain of medicine.

The report of the hitherto unsuspected occurrence of pellagra in the United States has excited widespread interest here in this disease, which has proven and still proves a veritable scourge in Italy and other European countries. In these countries pellagra is described as a chronic disease characterized by an erythematous exanthem, gastrointestinal phenomena and nervous and

psychic disturbances. It is generally regarded as an intoxication due to the using as food the products of unsound Indian corn. "Possibly the specific toxic products are formed by the action of some bacterium on maize which has been cut while immature and stored in damp condition " (Novy). In view of the extensive use of the proverbial "hoe-cake" as food in the South, it is rather surprising that pellagra should have so long escaped the notice of physicians. The report of its endemic occurrence in Alabama, North Carolina, South Carolina, Georgia, Mississippi, Florida and Texas, makes the study of the disease a matter of great importance.

Notwithstanding the immense amount of work which has been done on beriberi, the specific cause of the disease remains unknown. The micro-organismal and food theories each still have their advocates. It may be noted that Frederick Pearce, from clinical and pathologic observations on epidemics of beriberi and epidemic dropsy in Calcutta and Howrah, strongly suggests the identity of these diseases.

The clinical syndrome which is commonly known as dysentery has been shown to be due to three distinct diseases; amebic dysentery, due to *Entamœba histolytica;* bacillary dysentery, due to *Bacillus dysenteriæ* (Shiga, Flexner and Kruse); and catarrhal dysentery, due to the action of one of several bacteria which produce a catarrhal condition of the large intestine (Strong). This knowledge has furnished the basis for the more intelligent prevention and treatment of these diseases.

Studies on Malta or Mediterranean fever have shown that this disease, capable of producing an immense amount of invalidism, has a wider distribution than was formerly supposed. Mainly through the researches carried on in 1904-05-06 by a commission appointed under the auspices of the Royal Society of London, our knowledge of the disease has been distinctly advanced.

It has been shown that the *Micrococcus melitensis* is constantly present in the blood of patients suffering from the disease; that it escapes from the body chiefly through the urine; that it is found at times in the urine of perfectly healthy individuals. It has also been demonstrated that domestic animals (chiefly goats) are frequently infected and that the disease is largely if not entirely acquired by the use of the milk of these animals as food. A distinct advance in the therapy of the disease has been claimed by Bassett-Smith from the use, in chronic cases, of a vaccine prepared from cultures of the organism isolated from the spleen during life.

The march of the "black death" has advanced throughout the civilized world, and at the beginning of this decade we see it lodged in Asia, Africa, Europe, Oceania, North and South America. Fifty-one countries of these continents have been infected and millions of lives have been destroyed. Hence it is that the brilliant achievements with respect to the conveyance of the *Bacillus pestis* should rank with the epoch-making discoveries of this period.

Bannerman has pointed out that Simond in India was the first to suggest the flea as the carrier of the disease. His work, however, was discredited by the first plague commission. Captain Liston, an assistant to that commission, seeing the possibilities of this theory, continued investigations along this line, so that when the second plague commission was sent out in 1905, this method of transmission seemed the most worthy of investigation. Their carefully planned experiments and painstaking execution of the same have resulted in the following conclusions:

1. "Pneumonic plague is highly contagious, but being rare (less than 3 per cent. of all cases) plays a very small part in the spread of the disease.

2. "Bubonic plague in man is not infectious and is entirely dependent on the disease in the rat.

3. "The infection is conveyed from rat to rat, and from rat to man, solely by means of the rat flea.

4. "Plague is usually conveyed from place to place by rat fleas brought by people in their baggage or on their persons" (Bannerman).

The outbreak of plague on the Pacific coast in 1907 was suppressed by the efficient work of the United States Public Health and Marine-Hospital Service under the direction of Dr. Rupert Blue. Still, in view of the difficulties in certain areas attending the destruction of rats and rat fleas, the question of protective inoculation against plague has been the subject of extensive investigations. The researches of Strong in Manila has resulted in the production of a vaccine from attenuated plague bacilli which promises to be of great practical importance.

One of the most far-reaching results which has come about as a result of the increased interest in tropical diseases is the importance which attaches to protozoology and helminthology as fundamental medical sciences.

The researches of Laveran, Theobald Smith, Councilman, McCallum, Ross, Dutton, Novy and others stimulated men like Calkins, Minchin, Stiles, Mesnil, Nuttall, Schaudinn, and Grassi to study more carefully the protozoa. Great principles have been announced, the influence of which on medicine it is difficult to estimate.

By study of these organisms Hertwig has been able to announce the Kern plasma relation theory, Goldschmidt the chromidial apparatus, Schaudinn the nuclear dimorphism—theories and principles which offer much toward the elucidation of the long vexed questions of the physiology and pathology of the cell. Weissman's doctrine of the immortality of the protozoa has been overthrown by the fact that sexual reproduction is necessary at some period of the life cycle to rejuvenate these organisms "depressed" by vegetative activity or otherwise.

A knowledge of these life cycles has been shown to be necessary for a proper classification of these organisms, and has established close relations between phyla heretofore supposed to be widely separated.

Of greater importance in so far as tropical diseases are concerned are the results of the study of protozoa and helminths as pathogenic agents. Indeed, Sir Patrick Manson has said that in the study of tropical diseases "the student's attention is confined almost entirely to protozoa and helminths, to the special vectors or media of these organisms, to their pathologic effects, and to the prophylaxis and treatment of the diseases they give rise to."

The observations of Lösch, Kartulis, and Councilman and Lafleur had long ago established the etiologic relationship of amebas to a characteristic form of dysentery prevalent in tropical and subtropical regions and frequently associated with abscess of the liver. These observations have been confirmed by numerous observers. Much confusion, however, has existed as to the nomenclature and taxonomic position of these organisms, and even some skepticism as to their pathogenicity. Cassigandro and Barbigallo had shown that the amebas occurring in man and fresh water amebas presented sufficient difference to justify placing the former in a separate genus—entamœba.

In 1902 and '03 Schaudinn from morphologic and biologic differences, as well as from their effect on animals, was able to separate them further into two species—*Entamœba coli,* a harmless commensal of the intestinal tract, and *Entamœba histolytica,* the pathogenic agent of amebic dysentery. In 1904 Stiles summarized the various views as to the relationship of disease and amebas found in the intestine of man justifying the nomenclature of Schaudinn for those who believe in a harmless and pathogenic species. In 1908 Craig, after a most exhaustive study of the subject, wholly confirms the views suggested by Schaudinn.

It must be noted that there are still some observers who hesitate to accept the division of the entameba into pathogenic and non-pathogenic forms. These differences of opinion would seem to emphasize the desirability of relying on the full life cycle of these organisms under natural conditions rather than morphologic differences observed *in vitro* for purposes of classification.

Among the most interesting advances of this period are the discoveries which have removed trypanosomiasis far beyond the mere economic importance which it heretofore had maintained. The discovery of a peculiar, wormlike, actively motile body in the blood of a patient by Forde in 1901 and named *Trypanosoma gambiense* by Dutton stimulated investigations with respect to this organism as a pathogenic agent. The first result was the discovery of a trypanosomatic fever of man, which came about through the investigation of Dutton and Todd in 1902, under the auspices of the Liverpool School of Tropical Medicine. Shortly afterward the discovery, by Castillani, of this organism in the cerebrospinal fluid of a patient suffering from sleeping sickness led to the discovery by Bruce and others that this disease is caused by the *Trypanosoma gambiense* and that trypanosomatic fever is the first stage of sleeping sickness.

The *Glossina palpalis* has been shown to be the chief agent by which the organism is transmitted. In spite of efforts to show that the trypanosome undergoes biologic development in the tsetse fly which would be expected from what is known of the life-history of other hematozoa, the insect intermediary seems to be only a mechanical vector. Of other advances made in trypanosomiasis, the successful cultivation of these organisms *in vitro* by Novy and his associates is of importance as furnishing a method of studying these organisms. The early diagnosis of sleeping sickness by gland puncture

is of the greatest importance for purposes of prophylaxis and treatment.

The rapid spread of the disease is a striking illustration of the "disseminating influence that modern travel and means of communication have on diseases formerly confined to limited areas." Advances have also been made with respect to the prophylaxis and treatment of the disease. As a result of the work in Zambesi in 1907 and 1908 by Allan Kinghorne and R. Eustace Montgomery the following means for preventing the spread of the disease have been suggested—control of native movements, segregation of cases, removal of villages from dangerous zones, clearing, education of the natives, personal prophylaxis destruction of the tsetse flies, their larvæ and pupæ. Koch further suggests the destruction of crocodiles, inasmuch as the tsetse flies subsist almost entirely on the blood of these reptiles in the neighborhood of the lakes. Atoxyl, an anilid of metarsenious acid, supplemented by antimony, promises to be of service in the treatment of the disease.

The spirochetes, a genus closely allied to the trypanosomidæ, have been the subject of much study both from the academic and practical side. The discovery that African relapsing fever is caused by a spiral organism which is conveyed from one individual to another by means of the tick *Ornithodorus moubata* (Murray) and the spirillæ of American fowls conveyed by a species of argas, as well as the already known relation of a spiral organism to European relapsing fever, and its possible conveyance by an arachnid, raised the question whether or not these organisms should not be included among the protozoa.

The brilliant researches of Novy and Knapp and Breinl would seem to clear up to some extent the confusion which has existed with respect to the spirochetes. It seems to have been shown that these spiral organisms, the Spirillum duttoni, and the Spirillum recurrentis are different species belonging to the bacteria and

giving rise to different kinds of relapsing fever in various parts of the world.

These studies have aroused much scientific interest, as at first glance they would seem to furnish an exception to the general law enunciated by Stiles in 1901, that "those diseases which are dependent on insects or other arthropods for their dissemination and transmission are caused by parasitic animals." It does not seem conclusively proven that these arthropods are biologic transmitters of these diseases; that they are not necessary for the development of the spirilla, as are the anopheles for malaria or the *Stegomyia callopus* for the hypothetical organism of yellow fever. The work of Ricketts on Rocky Mountain Spotted Fever is also interesting in this connection, in addition to being a work of great merit.

Malaria, of all tropical diseases, is the most widespread, the most disastrous in its effects, and the one concerning which our knowledge was most complete at the beginning of this period. Hence it is that the application of this knowledge in the prevention of the disease has attracted the most attention. It should be noted, however, that the introduction of eosinated methyl azure stain and thick dehemoglobinized smears have facilitated the diagnosis of malaria. Schaudinn's discovery of the parthenogenetic cycle of the macrogametocyte in the blood of the vertebrate host furnishes a long desired explanation of the relapses which so frequently occur in this disease. Craig's more recent work on latent malaria should also be noted.

Much work has been done in various regions on the epidemiology and prophylaxis of malaria. Worthy of special notice are the researches and efforts of "The Society for the Study of Malaria in Italy." Professor Celli, in a report on this work, concludes that the campaign against malaria should include two methods concurrently—the one directed to destroy, or at least render inoffensive, the mosquito which inoculates man with

the parasite; the other directed to destroy with specific means and with general means these parasites in the human blood.

The recent excellent articles of Deaderick of Arkansas well present the present state of our knowledge as regards blackwater fever. While the results of investigators in various parts of the world seem to show the relation of malaria and quinin to the disease, the immediate cause of the condition which determines the increased hemolysis remains to be found out. The results of the researches of the medical commission of the United States Army to investigate the cause and mode of transmission of yellow fever are well known. And the application of this knowledge has been successful in the control of many outbreaks of the disease.

The work of E. H. Ross in Egypt, and Craig and Ashburn in the Philippines, would seem to indicate that dengue is dependent on the mosquito for its spread, and, therefore, another trophy is added to the war waged against these insects.

It has been shown that the presence of intestinal parasites has a marked influence on the mortality of other diseases, and the advances with respect to helminths as pathogenic agents are scarcely less notable than those with reference to the protozoa. Of the long list, time permits reference only to ankylostomiasis. This disease has been shown to be of wide distribution in all tropical and subtropical countries and wherever found is of the greatest importance from the economic as well as from the standpoint of public health. New hookworms have been discovered, their mode of infection has been determined, and much has been added to our knowledge of their clinical and pathologic manifestations. The ankylostoma duodenale has been shown to contain a hemolytic substance, and efficient methods of prophylaxis and treatment have been worked out. With all this, however, the work on hookworm disease may be said to have only begun.

This short and imperfect review serves to emphasize the great interest which has been manifested all over the civilized world in the study of tropical diseases during the past decade; to emphasize how vital the thorough study of these diseases is to the progress and art of medicine. There is already abundant cause for praise of the results which have been achieved, but it would seem that they are only evidence of what is to follow.

Without disparagement of the work of every and all nations concerned, we can with pleasure note the prominence of the influence of English thought in this as in other branches of medicine, and may be permitted to contemplate with pardonable pride the triumphs of America in this field.

The philanthropic spirit which moved the United States to engage in war to relieve a down-trodden people from the consequences of despotism was also sufficient to stimulate efforts to overcome a more formidable tyrant; to free these people from disease and pestilence. The establishment of a biologic laboratory in Manila as a part of the government laboratory and the high class of work which has emanated from this laboratory have reflected great credit on American medicine. The record of ten years of sanitation in the Philippines, of the scientific methods by means of which diseases have been combated, reads like a romance and justifies the statement of Musgrave that "America has made Manila one of the cleanest and healthiest and most attractive cities under the flag."

The discoveries with respect to yellow fever by the commission under the auspices of the War Department ranks as the greatest triumph of modern medicine since the discovery of vaccination against smallpox. As regards the triumph of America in the canal zone, it has been said that "of one credit history can not rob the United States. Among much good and evil it must record that it was under the American administration

that the knowledge and resources of modern medicine were applied to the hygienic redemption of the once noisome isthmus. Such fruits of labor in this direction have already been gathered that they promise to rival as a worthy monument of American achievement the canal itself." Leigh.

It is proper that we recognize the ability, revere the heroism and extol the genius of those who have brought about these and other triumphs. The names of no greater heroes will be recorded in the annals of American history than the names of Reed, Carrol and Lazear. Carlisle has said that genius is "infinite capacity for taking infinite pains." Measured by this standard the work of Colonel Gorgas in Cuba and Panama must stamp him as a genius whom we are proud to honor.

While we felicitate ourselves over this foreign missionary spirit and rejoice in the inestimable benefits which it has developed, we are led to inquire if the conditions are not such as to offer opportunities and impose obligations to increased activity in the field of home missions? If we consider only the great economic losses, the suffering, deaths, and race deterioration which amebic dysentery, malaria, and uncinariasis visit on this country, there can be but one answer. Unfortunately the vital statistics do not give a proper conception of the prevalence of amebic dysentery in the United States. Its wide endemic occurrence is, however, well known through the writings of Harris, Dock, Jelks, and others. Professor Osler says, "It is the most common variety of dysentery throughout the United States. It is endemic, the cases sometimes increasing to such an extent as to form an epidemic." Boggs states that the records of the Johns Hopkins Hospital show 182 cases in that institution from 1889 to 1908, the vast majority coming from the state of Maryland. He also points out that the large number of cases of abscess of the liver in the records of some southern hospitals would indicate its wide prevalence. The economic im-

portance of amebic dysentery, its chronicity, its resistance to treatment, as well as its tendency to serious complications, furnish a rich opportunity for investigation.

The prevalence of malaria is too well known to require discussion. Attention has often been called to its economic importance to a large section of this country. Woldert has shown that it cost the state of Texas in 1900 in loss from labor alone $533,320. Glenn W. Herrick, some years ago, in writing on the effect of malaria on agriculture, has convincingly shown the enormous losses which the disease entails on the South. More recently Howard, in a bulletin on the economic losses to the people of the United States through insects that carry disease, estimates on a very conservative basis that malaria produces 12,000 deaths and 3,000,000 cases of fever annually. He further states: "Accepting this as a basis and including the loss through death, the cost of medicine, the loss to enterprises in malarious regions through the difficulty of securing competent labor, and other factors, it is safe to place the annual loss to the United States from malarial disease under present conditions at not less than one hundred millions of dollars." To say nothing of the physical suffering and deaths, the losses from this disease alone make that from hog cholera, Texas cattle fever, and the boll wevill combined look exceedingly small. The above estimate of Howard does not include the retardation to development of certain regions on account of malaria. No region on earth more urgently invites the "triple alliance of the doctor, drainage and agriculture" than the great Mississippi Valley designated by one of its most gifted sons as "the cornucopia of the world." History, ancient and modern, furnish ample evidence of the baneful influence of malaria on mental and physical development.

Through the researches of the United States Public Health and Marine-Hospital Service, of the Porto Rican Commission, as well as of practitioners in the

endemic areas, we have learned of the great economic importance of the hookworm disease. According to the report of Surgeon General Wyman, the recent researches of Stiles have shown that 12.6 per cent. of the employés of the cotton mills of the South are affected with uncinariasis; that of this class 13 to 18 per cent. of those of maternity age are in a condition which prevents them from properly nourishing babes; 5.8 to 20 per cent. of the males of possible military age are in a condition which would materially decrease their military efficiency; 48.1 per cent. of the children are suffering from an anemia-producing disease which would naturally inhibit their usual capacity for study. These figures serve to emphasize the truth of the statements of Allen J. Smith, who, writing on this subject in 1904, said, "All through the districts of our southern states infested by the American hookworm there exists a class of persons notorious for their unprogressiveness, lack of ambition, application and effort, thin, sallow, unhealthy look, cadaveric appearance, and uniform poverty in the midst of natural fertility and plenty." He further states: "These families are usually prolific, but with parents of the type mentioned there are bound to arise numerous causes for fatality among the children. Probably many in childhood die from direct and indirect effects of uncinariasis. Of those who live a large, proportion suffering in some degree short of fatality from the same parasite, grow up stunted in mind and incapable of physical effort, without incentive, hopeless, unequal to real exertion, branded as lazy and wearing the mark without care or shame. These pallid, spindle-legged, pot-bellied, and always dirty and unkempt children grown to manhood and womanhood may scarcely hope to breed a stronger race than themselves; and thus, generation after generation, from originally strong and virile progenitors, families recede and eventually die out."

These are but examples of the opportunities afforded in tropical diseases at home. To these may be added the menace from bubonic plague, the ever-constant danger from yellow fever, and the probable endemic existence of other of these diseases which increased knowledge is demonstrating. Our increasing commerce with the tropics and the better facilities for communication with the same must inevitably increase these opportunities.

It follows as a natural corollary that these present and growing opportunities for the study of tropical diseases must impose the obligation of affording better facilities for teaching them and research work in them. If they are of such importance as we have indicated, it would seem that more time should be given to them in the curricula of our medical schools than is at present devoted to them. Even with this, the time has arrived when to keep in the front rank of the armies which are moving on these common enemies to our health and prosperity, the obligation rests on us to follow the examples of England, Germany, France and other countries in the establishment of an institute for the study and teaching of these diseases, Dr. E. N. Tobey, of the Harvard Medical School, has, in recent articles, successfully answered the objections which have been urged against this necessity.

The need for a special institute for the study of tropical diseases is in no sense a reflection on the magnificent work which the Bureau of Public Health and Marine-Hospital Service has done and is doing. The sharp eye which this service keeps on our ports to prevent the entrance of exotic disease, the magnificent service which it has rendered in the suppression of pestilences, the importance which the hygienic laboratory has assumed as a center of research in contagious and infectious diseases, the pioneer work which it has instituted with respect to the study of leprosy amongst other labors, compels us to agree with Seaman when he says

that "the United States Public Health and Marine-Hospital Service is the one department of which Americans have most reason to feel justly proud."

The growing sentiment in this country of the obligations of the federal government to the public health is propitious, and this sentiment needs the fostering care of physicians more than any other class. The importance which we to-day assign to tropical diseases in this country demands our best efforts in the extension of the authority of this service and in the securing of appropriations to render it still more efficient.

Let us hope that these opportunities will impel the performance of the duties which they impose.

THE PRESENT STATUS OF THE SERUM THERAPY OF EPIDEMIC CEREBRO-SPINAL MENINGITIS

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My intention is to present a very brief statement of the status of the serum treatment of epidemic meningitis. It is now about three years since the serum was first used therapeutically in this country. Gradually its employment has extended until now it is being used in Great Britain, France and Germany, as well as in the United States and Canada. Indeed, the Rockefeller Institute has sent supplies to India and to Jerusalem, but, as no reports have been received from these distant places, they will not be further considered at present.

At the time of the first employment of the serum in this country the epidemic of meningitis had already receded in the East, and, although the disease spread westward even beyond the Rocky Mountains and was often very severe and fatal, yet the number of cases arising or being recognized in any one community was not large. I, therefore, view the test made of the serum in America as having coincided with the period of recession of the epidemic.

At the period of the first employment of our serum in Belfast and Edinburgh the epidemic was at its height; that is to say, it had reached its maximum development, from which it was tending to recede rather than to extend. All the evidence at hand shows that the disease at that time had not diminished in virulence and

fatality, but the number of cases appearing was in a given time less than before.

In Germany, also, the epidemic was virtually at an end when the serum was received. In France, on the other hand, the serum was available at the beginning of the outbreak of the epidemic which is now prevailing in Paris and the provinces. To the fortunate circumstance that Professor Calmette, on his return from the International Congress on Tuberculosis, carried with him to Lille a considerable quantity of the serum is to be ascribed its prompt employment. Subsequently the Rockefeller Institute sent large supplies to him, to Professor Netter and to Professor Roux. The reports of the serum treatment now appearing in French medical journals are based chiefly on the employment of the serum prepared at the Rockefeller Institute.

If, therefore, the decision of the value of the serum treatment was properly withheld until the opportunity arose to subject it to a test at the beginning of a severe epidemic, when the fatality is commonly at its height, this opportunity has now arrived in France. The outlook is further promising for a comparative study of cases of epidemic meningitis treated with the serum and in other ways. While the serum is being employed widely, apparently, in Paris and in the intense way that experience has indicated to be the best, namely, by successive injections of relatively large doses, in the provinces it is being less generally employed and it has been found difficult to have the intense method carried out by the provincial practitioners. When the reports are all in and the figures have been collected we may expect, therefore, valuable information on the value of the serum.

In the meantime, I can report to you that the excellent results obtained from the serum in America and Great Britain are being repeated in France. There have already been published reports covering 100 or more cases of the disease treated with the serum in which the

mortality will probably be less than 25 per cent. On the other hand, a smaller number of cases thus far reported treated by other methods have given a far greater mortality and one approaching 80 per cent. Moreover, the phenomena of diminution in severity of the symptoms and reduction of the period of infection and convalescence have been observed there as elsewhere.

We may, then, consider fairly, I think, that the serum treatment has now been subjected to test under a variety of conditions, some of which were as severe as probably ever occur. And yet I should still advise caution in concluding that the case has been proved for the serum. The total number of reports of cases of epidemic meningitis treated with the serum prepared at the Rockefeller Institute which I have collected is under one thousand, and it obviously will take a larger number than that to establish its value. I wish now to present a tabulation which has recently been prepared based on 712 cases of the disease in which the bacteriologic diagnosis was made and the serum treatment used. In the first table the cases are subdivided according to certain age periods, and in the second the total cases of each age period are further subdivided according as the serum was injected in the three arbitrarily chosen periods of duration of the disease.

TABLE 1.—CASES OF EPIDEMIC CEREBROSPINAL MENINGITIS TREATED WITH THE ANTIMENINGITIS SERUM

CASES ANALYZED ACCORDING TO AGE GROUPS

Age years.	Total no. cases.	Recovered.	Died.	% Mortality.
1-2	104	60	44	42.3
2-5	112	82	30	26.7
5-10	113	95	18	15.9
10-15	101	73	28	27.7
15-20	107	72	35	32.7
20+	175	106	69	39.4
Total, all ages	712	488	224	31.4

Table 1 brings out several points of interest. The highest mortality is shown to have occurred in the first two years of life. But contrary to the rule under the older forms of treatment in which the mortality was 90 per cent., or over, in this series it was 42.3 per cent.

The second age period is from 2 to 5 years, in which the mortality was 26.7 per cent. The third age period embraces children from 5 to 10 years of age and gave the lowest mortality of all, namely, 15.9 per cent. The next period extends from 10 to 15 years and gave a mortality of 27.7 per cent. The next period of from 15 to 20 years showed a considerable rise in mortality, equaling 32.7 per cent., and the last period, embracing the cases of 20 years and over, gave a mortality of 39.4 per cent. The average mortality in all the age periods was 31.4 per cent.

The time allowed me is insufficient to enable me to enter into a detailed discussion of the figures. It is my intention, however, to consider them in some detail in the near future. A point of importance and one to which Dr. Jobling and I have already referred is the importance of experience with the serum in securing the best results from it. If the separate large series of cases treated by individual observers are analyzed, the great discrepancy in the results as between children over 2 years of age, young adults and adults past 20 years are not encountered.

TABLE 2.—CASES OF EPIDEMIC CEREBROSPINAL MENINGITIS TREATED WITH THE ANTIMENINGITIS SERUM

CASES ANALYZED ACCORDING TO DAY OF INJECTION

	Period of Injection—Day.								
	1st-3rd			4th-7th			Later than 7th		
Ages. Yrs.	Rec.	Died.	%	Rec.	Died.	%	Rec.	Died.	%
1-2	16	1	5.8	22	10	31.2	22	33	60.
2-5	24	6	20.	40	12	23.	18	12	40.
5-10	43	8	15.6	35	6	14.6	17	4	19.
10-15	36	8	19.	23	9	28.1	14	11	40.
15-20	25	17	40.4	25	8	24.2	22	10	31.2
20+	36	21	36.8	34	24	41.3	36	24	40.
Totals..	180	61	25.3	179	69	27.8	129	94	42.1

Table 2 is instructive in bringing out the importance of early injections of the serum. The results in the first two years of life are especially noteworthy. The extraordinary figures given under the first period of injection, namely, in the first three days of the disease, can hardly be maintained. But the influence of period of injection

is shown by the rapid rise in mortality in the subsequent two periods. The rule of the effects of early injection is preserved in the age periods up to the period of from 15 to 20 years, when it disappears. The discrepancy occurring in the two highest age periods cannot be wholly accounted for at present. The explanations which suggest themselves are that among older individuals there tends to be a large number of very severe, rapidly fatal or fulminating cases of the disease, or that older persons are less subject to the beneficial action of the serum. As regards the actual proposition, it may be stated that adults not infrequently respond promptly to the serum injections by abrupt termination of the disease or ameliorated symptoms and pathologic conditions.

The total figures do not, however, fail to indicate that the early injections are more effective than the later ones, as is shown by the percentage mortality in the first-to-third-day period of 25.3, in the fourth-to-seventh-day period of 27.8, and the period later than the seventh day of 42.1.

There is one consideration which I should like to touch on. The study of certain groups of cases of epidemic meningitis, coming under one observer, indicates that the diagnosis can sometimes be made before the usual symptoms of meningeal irritation appear or are recognizable. The cerebrospinal fluid removed by exploratory lumbar puncture has been, in these cases, sometimes clear and sometimes turbid and contained more or less polynuclear leucocytes and always *Diplococcus intracellularis*. The serum being injected immediately, these cases almost invariably were abruptly terminated or ran relatively a mild course. Attention having been drawn to the cases as being possibly examples of epidemic meningitis because of the similarity of the prodromal symptoms to those of other cases diagnosed later after the signs of meningeal irritation were plain, they ran a short and mild course after the early administration of the serum, while the others, which

served to direct the attention, having been injected later when the infection and inflammation were well established, assumed a far more severe and protracted form.

Rockefeller Institute for Medical Research.

ABSTRACT OF DISCUSSION

DR. THOMAS MORGAN ROTCH, Boston: In my wards at the Children's Hospital during the last ten years, I have had on an average twenty of these cases each year. The children treated were in the first twelve years of life and I have carried out a different form of treatment during each of the past six years. During 1899, 1900, 1901 and 1902 no special treatment was employed and the mortality varied from 60 to 80 per cent. During 1903, 1904 and 1905 the treatment was by repeated lumbar punctures and the mortality continued from 60 to over 70 per cent. Although the lumbar punctures produced no notable change in the percentage of deaths yet a certain temporary amelioration was noticed at times. During 1906, all the children were treated with diphtheria antitoxin, the doses varying from 115,000 to 144,000 units according to the age of the child. An analysis of these cases showed no especially favorable results, the mortality being about 80 per cent. During 1907, in connection with my work on the opsonic index the treatment was with the vaccines and the mortality still remained up to about 80 per cent. In all the nine years from 1899 to 1907 the mortality varied from 60 to 80 per cent.

From Nov. 1, 1907, to Nov. 1, 1908, the Flexner serum was employed and the mortality immediately fell from 80 to 19 per cent. This lower rate of mortality has varied a little since Nov. 1, 1908, but has never gone above 25 per cent.

The technic of the serum treatment in these 74 cases has been carried out by Dr. Charles Hunter Dunn. The amount of serum given varied according to the case but from 30 to 45 c.c. at a dose was found to be safe, given daily for at least four days. It is seldom that too much serum is given. In one patient, a small baby, symptoms of cyanosis, irregular respiration and collapse occurred but the symptoms soon passed off and in the Dunn series only one other child was affected and this not seriously.

The mistake which is most likely to be made is the giving of too little rather than too much. It is also a mistake to stop repeating the dose until grave symptoms return. The serum should be repeated at least once a day and in grave cases oftener until not only all symptoms have disappeared, but until the organisms are no longer found in the spinal fluid. Reports as to the results do not give a fair idea of the value of the serum treatment unless the technic is carried out in the most perfected way. In this series of 74 cases the

technic was carried out with the greatest precision with the method approved by Flexner.

The serum treatment should not be mistrusted or given up because certain patients do not respond to it. There are two reasons why some individuals do not respond to the serum: 1. Because in some cases it is probable that the serum can not reach certain parts of the brain infected. For instance, if by the inflammatory process brought about by the disease the foramen of Magendie has been closed the organisms may still be active while enclosed in the ventricles where the serum can not reach them or in like manner perhaps in some remote

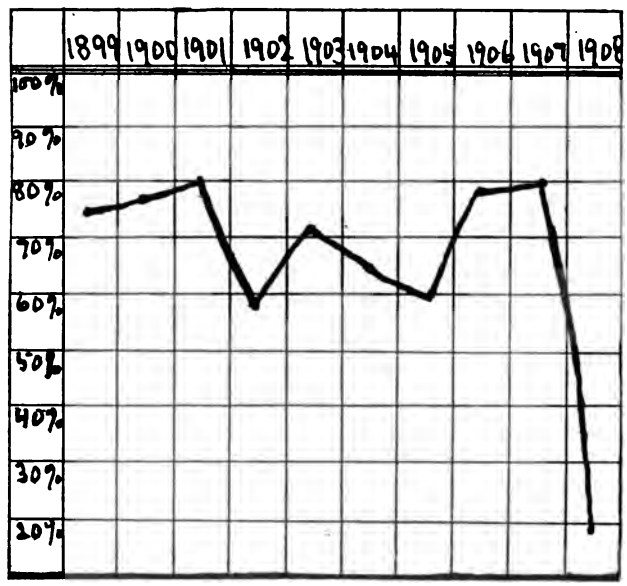

Chart showing death rate from epidemic cerebrospinal meningitis at the Children's Hospital, Boston, from 1899 to 1908.

cerebral sulcus. 2. It has not been proved that there are not a number of strains of *Diplococcus intracellularis*, some of which may be resistant to the serum.

In those cases in which an individual does not respond to the serum, cultures from the spinal fluid should at once be sent to the Rockefeller Institute in order that Dr. Flexner should be enabled to investigate this possibility and perhaps later be able to increase the polyvalent property of the serum by including them in immunizing his horses. Analogous to these characteristics of the *Diplococcus intracellularis* is the well-known efficiency of certain strains of the lactic acid bacil-

lus and the uselessness of others on certain fermental saprophytes in the intestine. The truth of these observations has been exemplified in Dunn's clinical work.

DR. PHILIP KING BROWN, San Francisco: Dr. Rotch's statement regarding the care of these patients in hospitals makes me wish to report a brief experience with the treatment of these cases in country towns in California where the disease seems to be endemic. It appears in epidemic form occasionally in small isolated communities. I wish especially to speak of this because of the remarkable results obtained in the use of the serum by the country practitioners and they should be given the credit of the work. I can not allow this opportunity to pass without speaking of it because of its bearing on the general use of the serum which I believe is bound to come. In all but one group of cases the serum was administered by the physician to whom I gave it, after I had made the initial injection. The most striking results occurred in one small town where eleven patients died before the serum was used. Then in a twelfth doubtful case the child recovered. The deaths occurred in periods of from five hours to four days after the onset of the initial symptoms. After the introduction of the serum, three patients promptly recovered. The fourth case died because the supply of serum gave out. A fifth patient from a distant place, ill two weeks before the serum was tried, recovered after the use of a number of doses of the serum. In a number of localities where I have gone to administer the first dose of the serum, I left a supply to be used by the local physician in the further care of patients and in subsequent cases that might arise. The best results obtained in California were obtained by the country doctors. In one late case the patient was deaf and nearly blind when the serum was begun; the sight returned to normal, but the hearing was not recovered. In another case the patient was almost blind before the use of the serum, but the sight was subsequently regained. Strange to say, the results in San Francisco were not so good as in the country towns. I did the work myself and did the best I knew how, but still I was not able to obtain the results obtained by the men in the country. Generally speaking, this seems to have been due to the late use of the serum, to complications and to the very bad hygienic surroundings in the homes of several of the patients. In no case, however, did I have to contend with the difficulties and disadvantages hygienically and as regards assistance in carrying out the treatment that attended all the cases I saw in the country towns and still my results were not as good as the country physicians'.

DR. WILLIAM LITTERER, Nashville, Tenn.: There has just been an epidemic of cerebrospinal meningitis in Nashville. The number of cases was 20, which was confirmed by bac-

teriologic examinations. Dr. Flexner kindly furnished us all the serum that we needed. In the first three cases in which the serum was not used, the patients died promptly. Out of the seventeen remaining patients in whom the serum was used, only 7 died; 3 of those who died were practically moribund when the serum was injected. The serum acted like magic on 2 moribund patients. Leaving out the moribund patients, 4 out of the 14 died.

We were particularly struck with two cases in which the meningococci were found in fairly large numbers in the fluid. After the first injection of the serum the number had decreased materially and by the third injection cultures were absolutely negative and the spinal fluid perfectly clear, yet the patients complained of agonizing headaches which were the chief feature of these cases. One of the patients died on the eighth and the other on the sixth day of the disease. I am of the opinion that the meningococci had extended into the ventricles of the brain and that the serum could not reach them. I am further of the belief that possibly we could have saved the patients had we injected the serum into the ventricles of the brain.

Dr. Simon Flexner, New York: There are two symptoms which are likely to persist after the disease has entirely yielded to the treatment, namely, rigidity of the neck and the Kernig sign. Other things being favorable, they can be disregarded, and may persist even for several weeks, and gradually disappear. A second point I should like to refer to is that apparently certain strains of the diplococcus are more resistant to the destructive and inhibiting influence of the serum already mentioned. How to explain this I do not know. I had intended to collect some of these strains for a special study, but have had little success in securing them thus far. The cases have occurred often in distant and widely separated places, so that the cultures of the resistant diplococci have not survived the journey by mail to New York, and so far I have not succeeded in securing such resistant strains in New York. I trust to pursue this investigation in the future.

I am confident that the inflammatory exudate is sometimes formed in inaccessible parts of the meninges, or in deeper parts of the brain where the serum can not reach. Then in cases of hydrocephalus the obstruction at the base of the brain often prevents the serum from reaching the cerebral meninges and ventricles, where the exudate is contained. Cushing of Baltimore first carried out intraventricular injection of the serum in children in whom this obstruction existed, after trephining the skull; and in young children it is possible to make the injection through the anterior fontanelle,

but up to the present time in no case of this kind, so far as I know, has the patient recovered. Whether better results will be obtained later can not of course be predicted, but in any event I think the operation justifiable, since these cases always terminate fatally.

Finally, I wish to express my deep sense of indebtedness to the large number of physicians, many of whom I have never met, for their hearty cooperation, which I appreciate very much, and without which this wide investigation could not have been made.

CARDIAC AND VASCULAR COMPLICATIONS IN PNEUMONIA

WITH SPECIAL REFERENCE TO TREATMENT

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If we glance at the etiologic conceptions which formerly existed in connection with lobar pneumonia—and unless otherwise stated lobar pneumonia is the only form of pneumonia referred to in this paper—it will not be difficult to see why the heart was neglected. Those who believed in a humoral origin of the disease assumed that the only thing requisite for the cure of pneumonia was blood-letting, and that it was not necessary to look to the heart. Indeed, with Bouillaud's formula of bleeding (1830), *coup sur coup* and withdrawing twelve to sixteen ounces at a time, the heart was literally neglected. Then came a time when bleeding was restricted to cases which presented some indication for it, although, as Trousseau says, most physicians and all the laity could not conceive of pneumonia patients recovering without it. The indication was not stated precisely, but more or less vaguely as, with Trousseau, general congestion. About the same time (1847) Skoda and Dietl (1847) pointed out the dangers, as well as the inutility, of the procedure in any case of pneumonia and substituted for it that which has been called the expectant treatment, or better, nihilistic treatment, which, however, was followed by more recoveries than had ever followed bleeding.

It was not until 1874, when von Jürgensen wrote his remarkable article,[1] that the heart was brought into prominence; he says: "The danger to life which croupous pneumonia produces in the patient first threatens the heart. Pneumonia death is caused by cardiac insufficiency." In this article, which in some ways is almost prophetic, he says, "Sine pulsu nulla therapia," thus differentiating pneumonia from typhoid fever, in which there is no treatment without the thermometer. Furthermore, among many other things now accepted, von Jürgensen recommends the fresh-air treatment, which has been so successfully rediscovered within the last few years.

About ten years after this (1884-5) A. Fraenkel discovered the cause of lobar pneumonia, namely, Fraenkel's diplococcus, the *micrococcus lanceolatus,* or as Fraenkel himself calls it, the pneumococcus. From this time our expectations of increased knowledge were fulfilled. For clinical and therapeutic purposes many things have been added, for the study of blood-vessel conditions the most important is found in Romberg and Pässler's contribution [2] on the effect of pneumonia infection on the general circulation. These two observers showed that the toxic albuminoid which is produced during metabolic activity of the pneumococcus paralyzes the vasomotor center in the medulla oblongata, and Pässler, in a subsequent communication[3] states that this is the most common cause of death in pneumonia, in as far as the circulatory apparatus alone is concerned. The objections to the complete acceptance of this view were that there was the incomplete accordance of experimental results and clinical observation, and that the condition had not been identified in man. At the present day the first

1. In von Ziemmsen's Handbuch der speciellen Pathologie und Therapie, vol. v, part 2.

2. Romberg, E., and Pässler, H.: Experimentelle Untersuchungen über die allgemeine Pathologie der Kreislaufstörungen bei akuten Infectionskrankheiten, Deutsch. Arch. f. klin. Med., 1895, lxiv, pp. 652-763.

3. Pässler, E.: Zur Behandlung der fibrinösen Pneumonie, München. med. Wchnschr., 1901, xlviii, No. 8.

may be considered as having been satisfactorily settled; for the second, although identification is fairly complete, much more must be done in order that the clinical picture may be accepted by the profession at large. I do not hesitate to state that with a healthy heart vasomotor paralysis is the most common cause of pneumonia death, in so far as the cardiovascular apparatus is concerned, and it goes without saying that this mode of death may occur irrespective of health or disease of the heart. As a matter of fact, there is still some doubt whether, with sufficient infection to produce this vasomotor condition, the heart muscle is not always affected and whether the former or the latter develops first.

Long ago it has been shown in animals that, on section of the splanchnic nerve, an enormous quantity of blood accumulates in the intestine, which is followed by intense anemia in other organs, especially in the central nervous system, which may cause death. The splanchnic nerve is the vasomotor nerve of the intestines, and its section causes paralysis of vasomotor function and enormous dilatation of blood-vessels. In paralyzing the vasomotor center with the pneumococcus the same result follows in man. In brief, in man there is first, dilatation of blood-vessels in the splanchnic area; the blood-pressure, which sooner or later is normally low in pneumonia, sinks; the heart, which is supplied by an insufficient quantity of blood, which is gradually becoming stationary in the affected area, continues to draw blood from other places, the liver, the skin, the muscles and central nervous system, and becomes more and more rapid and ineffectual, "bleeding itself into the splanchnic area," and finally stops. The intracardiac pressure is reduced so that the myocardium ceases to contract; moreover, the various cardiac and vasomotor centers become asphyxiated, and therefore paralyzed.

All this, as Pässler first pointed out, produces a characteristic clinical picture. My observation has led me to add to his description, so that it presents itself as

follows: The first evidences are rapidity of heart and sinking of blood-pressure; with this, or shortly afterward, there comes tympanites; the patient then presents an exsanguinated appearance, with beginning evidences of collapse; the pulse becomes irregular, empty and so rapid that it cannot be counted; symptoms of cerebral anemia begin to appear—delirium, hallucinations, sometimes great restlessness; they gradually disappear to be superseded by stupor and coma; the collapse increases; the heart becomes more irregular; the heart sounds disappear, and the patient dies.

With such an appalling possibility staring us in the face in every case of pneumonia (for we are not in a condition to determine when the infection is sufficient to produce the condition described), it would seem natural to resort to means in order that its development may be prevented. In order to accomplish this purpose A. Fraenkel[4] recommends the administration of digitalis. He gives ¾ gm. a day for three or four days, maximum 12 gm. in all, in all cases which come under observation within the first three days of the disease. It is contraindicated in patients with organic disease of the heart, kidneys or blood-vessels, and he does not apply this mode of treatment in drinkers and patients over 50 years of age. His results seem to be satisfactory; the temperature sinks; the pulse does not become more rapid and the blood-pressure never diminishes. Theoretically there can be no objection to this mode of treatment, but my own experience with it has not convinced me that it is the best. In 1891 Petresco[5] of Bucharest published an article on the treatment of pneumonia with large doses of digitalis in which he recommends the administration daily of 4-8 gm. of digitalis infusion given in twenty-four hours, according to the severity of the case. In some cases he gave as much as 24 gm. in four to five days. As there was an epidemic of pneumonia in my

4. Fraenkel, A.: Spezielle Pathologie and Therapie der Lungenkrankheiten, 1904, ii, 372.
5. Petresco: Therap. Monatshefte, 1891, p. 121.

wards at the time of the appearance of this publication, all the patients were put on this treatment. I failed to verify nearly all of his conclusions, even to the small detail that the pulse fell after one to three doses had been given. On the contrary, mortality was greater than before. All the evil effects that can be produced by digitalis were noted, and after three days of administration of the remedy such cumulative effects were produced as I shall hope never to see again.

The next remedy which I tried was the routine administration of strychnin; while I should not want to be without it in the acute infections, it does not prevent the vasomotor syndrome which is under consideration.

Because of the peculiar action of caffein, in stimulating the vasomotor center and its action on the heart, I have administered this drug for the last twelve years in a routine way. Caffein always increases blood-pressure, unless there is some organic lesion which in and of itself produces increased blood-pressure. Thus, in nephritis, when the pressure is abnormally high, it is doubtful if the pressure goes higher on administration of caffein, but the presence of this complication is, it seems to me, an additional reason for giving the drug.

In aortic sclerosis and splanchnic sclerosis caffein may be given with safety when the blood-pressure is below normal, or when it sinks. In all organic heart lesions it is also safe. So that the only contraindication for its use would be abnormally high blood-pressure, when there is danger of doing harm by the possibility of increasing it, a condition which may present itself in cases of cerebral arteriosclerosis, or in recent endocarditis. I have never seen any other effect on the heart than diminution in rate in pneumonia when the drug is given in proper doses. For prophylactic purposes it is not necessary to give more than 0.10 to 0.30 gm.—(gr. i ss to v) every four hours. When the symptoms of "bleeding into the splanchnic area" have developed it should be given hypodermically 0.20

gm. three or four times daily. I employ the double salts (preferably the caffein-sodiosalicylate because it is best made in this country), as they are more stable when dissolved in water, more soluble and less irritating when administered hypodermically than any of the other salts of caffein. On the whole, they do exactly what Fraenkel has claimed for digitalis; they reduce the pulse-rate, the fever may become reduced; they increase the blood-pressure; they reduce the mortality without being subjected to many limitations in administration and without producing the unpleasant effects of digitalis when given in proper dosage. Occasionally it occurs that patients become nervous and sleepless, which is remedied by reduction of dose.

Other preventive measures of great importance should also be considered. First among them I would place the fresh-air treatment, which reduces wear and tear, rendering all patients less liable to fatigue and which also lessens toxemia. Next to this, I would emphasize the necessity of treating sleeplessness from whatever cause it may arise; the continuance of wakefulness is very dangerous, both for the nervous system and for the heart, and as von Jürgensen says, "there are cases in which the whole therapeutic problem temporarily reduces itself to the production of sleep." Lastly, it may become necessary, in individual cases to reduce the temperature. I have purposely said "individual cases," as antithermic treatment is not necessary, as a rule. When the temperature produces damage it should be reduced, but only by such measures as do no harm, and especially do no harm to the heart.

The Nauheim or calcium chlorid baths, as recommended by P. K. Brown,[6] in vasomotor paresis in acute infectious diseases might be advantageously employed instead of the ordinary cool or cold bath, especially as a preventive measure. Besides these, all those other dietetic, hygienic and therapeutic measures and the

6. Brown, P. K.: Tr. Assn. Am. Physicians, 1906, xxi, 641.

proper treatment of other symptoms must be considered as acting prophylactically, notably those which may affect the central nervous system unfavorably.

When the symptom-complex has developed then most energetic measures should be adopted. In 1898 I was successful in arresting a case of splanchnic vasomotor paralysis, and in 1904, after having had a number of cases, two of which were in children, I published the method[7] which had been successful. It is as follows: Adrenalin is employed for the purpose of contracting the blood-vessels of the spanchnic area, for which, according to Abel, it has an elective affinity; hypodermoclysis or venous transfusion with large quantities of normal saline solution (0.90 per cent. Hamburger) for the prevention of asystole, one or two ice-bags on the abdomen which reduce the pulse, probably by stimulation of a splanchnic reflex. Adrenals were first recommended in pneumonia by E. A. Gray[8] in 1902. Henry L. Elsner[9] recommends adrenalin for vasomotor paralysis for precisely the same reason as stated above. Adrenalin may be given with the hypodermoclysis, 1 c.c. of a 1000 solution; the frequency of its application must depend on the symptoms, as its effects are transitory. This is one of the few conditions in which a physician should be "in constant attendance." According to the rate and rhythm of the pulse, which are entirely satisfactory indices, even without blood-pressure estimations in the onset, the drug should be administered every two to four hours. This cannot be kept up very long, so that I have found it necessary to give hypodermic injections of caffein to take the place of the hypodermoclysis, which usually results in giving three or four saline and adrenalin injections a day and four doses of caffein. In the first twenty-four to thirty-six hours most reliance

7. Forchheimer, F.: Acute Myocardial Insufficiency, Arch. Pediatr., 1904, xxi, 684.
8. Gray, E. A.: The Influence of Suprarenals in Pneumonia. Med. Rec., 1902, lxi, 527.
9. Elsner, Henry L.: Treatment of Cardiac Asthenia of Pneumonia, New York Med. Rec., 1904, lxxix, 12.

should be placed on hypodermoclysis; with the added adrenalin gradually the caffein is allowed to take its place. The ice-bags are valuable adjuncts; in one patient, without any other treatment, I succeeded in reducing the pulse-rate from 140 to 60 per minute. As soon as such an effect is produced, or when tympanites disappears, the ice-bags should be discontinued, to be reapplied when the pulse goes up or the tympanites reappears. This mode of treatment, applied in all kinds of vasomotor paralysis, has given me about 50 per cent. recoveries. Esser[10] has employed large doses of camphor hypodermically to increase blood-pressure; in one case he gave 23 gm. (345 grains) in four days. He lost 2 cases out of 13—but his record is not perfectly clear, as 2 cases, at least, belonged to another type of heart failure.

The subject of dilatation of the right heart as a menace in pneumonia has received considerable attention by modern writers. Those of us who have seen a great deal of pneumonia will admit that it is a rare occurrence. A. Fraenkel[4] states that it cannot be found in all serious cases. Petzold[11] records observations in 271 cases without having found it once. Pässler[8] claims that it may occur in rare instances from increased resistance in the pulmonary circulation. On the other hand, all pathologists point out the fact that after death the right chamber of the heart is distended by firm coagula. But, as it *is* admitted to exist by clinicians, it seems unnecessary, at this time, to discuss the apparent discrepancy between clinical and the pathologic-anatomic attitudes; we certainly must admit with A. Fraenkel that if the heart is not too unfavorably affected by toxic effects, resistance in the pulmonary circulation "is overcome without difficulty and without dilatation of the right heart in the greatest number of cases."

10. Esser.: München. med. Wchnschr., 1904, li, 2314.
11. Petzold: Deutsch. Arch. f. klin. Med., lxx, 373.

The clinical picture differs altogether from that produced by vasomotor paralysis. The patient is cyanotic; there is great dyspnea; increased activity of all the obligatory as well as accessory respiratory muscles, as well *as by* all the other evidences of dyspnea are present. On examination we find the jugular veins overfilled, the movements of the heart very much increased, especially those of the right ventricle; on percussion there is increased heart dulness to the right from 1 to 3 cm.; on auscultation there is accentuation of the second pulmonary sound which disappears as the case progresses. Frequently edema of the lungs is also found. The liver is usually enlarged; when the condition lasts for over twenty-four hours it is very much enlarged. The patient dies in asphyxia—never in collapse, unless this condition is combined with vasomotor paralysis. The simplest treatment of this condition is blood-letting by venesection, and ordinarily from eight to sixteen ounces should be drawn. Primarily the pulmonary circulation is relieved, and, secondarily, the dilatation of the right heart. If there is pulmonary edema this may also disappear; at all events when done properly, phlebotomy is followed by remarkable results, so remarkable, indeed, as to make one wonder if blood-letting has not become what Gross called it, a lost art. It is, however, not necessary to do this in every case. The mode of treatment which is applied in ordinary cases of acute myocardial insufficiency is usually sufficient. It consists of hypodermic injections of digitalin in large doses, of camphor and ether, of caffein. Alcohol is not indicated unless the patient is an alcoholic.

The other cardiac conditions which may develop in the healthy heart are pericarditis, acute myocarditis and endocarditis. Endocarditis is the most frequent complication, and the third most common cause for pericarditis is the pneumococcus. In regard to acute myocarditis in pneumonia our knowledge is fragmentary. Without any other cause the frequency of pericarditis and endo-

carditis would lead one to imagine that acute myocarditis should also be present. But from what we know of the etiology of acute myocarditis this could not be final, as we find acute myocarditis in pneumonia, without either pericarditis or endocarditis. It seems, however, that acute myocarditis in pneumonia is the postfebrile form and as such leads to sudden death from acute myocardial insufficiency. Acute endocarditis is found as the simple and the septic form (malignant, ulcerative endocarditis). As pneumonia is a bacteriemia, it is not remarkable that the septic form develops with relative frequency. The treatment of these conditions is the same as is applied to them under other conditions.

From von Leyden's statement it seems that we in America, as well as the Russians, have taken to employing strychnin in the heart complications of pneumonia and, as he says, he also has employed it with benefit. As far as the heart is concerned, strychnin has an effect only in toxic doses. Indirectly given in normal doses it may, however, affect the heart by stimulating its inhibitory center, and, therefore, reducing its rate. It furthermore is followed by contraction of blood-vessels, but, in man, not sufficient to increase blood-pressure. As strychnin increases the irritability of the cord somewhat, many of the normal functions of the cord are increased in activity. Furthermore, it stimulates the respiratory center, in normal doses, but large doses are followed by paralysis. It would seem, then, that when we give large doses, so frequently administered in pneumonia in a routine way, we may stimulate the heart, but do great damage to the respiratory center. In small doses it is invaluable in pneumonia, in acute myocarditis, although it has also been given in enormous doses here with apparent success, but it is especially valuable as a stimulant of the respiratory center—indeed, as a stimulant of the whole cord. On the other hand, its routine administration, especially to the degree of producing toxic effects, should not be encouraged, as it does not

prevent the accident we now most fear and, moreover, produces deleterious effects. Elsner[9] most forcibly states the position in regard to the administration of nitroglycerin in a healthy heart; we already have lowered blood-pressure; why should we increase it, and bring it to or beyond the danger line? It should not be given, even in overfilling of the right ventricle, as it especially affects the splanchnic area.

The treatment of pneumonia with coexisting heart disease has been variously described. Some authors give digitalis in every case, others only for specific indications. It would seem that as in routine administration of digitalis in any heart disease this drug might do harm, as it does when administered indiscriminately. With the present advance which we owe to modern pharmacy, in giving us reliable glucosids, acting when given in proper doses, either hypodermically or intravenously, with certainty and promptly, the preparation of the heart for a possible breakdown, which takes at least two days, is no longer necessary. At least such has been my experience in the last three or four years. In chronic valvular disease in which I always gave digitalis formerly I now restrict its administration to those cases in which there is a probability of decompensation because of the additional work put on the heart. The conditions may be summed up as follows, such as have already had decomposition or are having it when pneumonia develops, and, furthermore, in those valvular lesions in which compensation is not complete. Therefore, in all valvular lesions, except aortic or mitral insufficiency in which there is complete compensation, it is not wise to take chances.

With diseases of the myocardium we find, on the whole, the most dangerous complicated form of pneumonia; Pässler's statistics show that in pneumonia with chronic myocarditis the mortality is 93 per cent. While I believe this to be an exaggerated statement, because of the small number of cases which are considered, it is,

nevertheless, true that chronic myocarditis is the greatest menace to life in patients with pneumonia. But here, as well as in all other forms of myocardial diseases, the degree of danger lies in the degree of existing chronic myocardial insufficiency. Any patient who goes into an attack of pneumonia with abnormally low blood-pressure due to chronic myocardial insufficiency has little chance for recovery.

Whenever any manifestation of myocardial insufficiency develops it should be treated as an acute myocardial insufficiency. The results naturally vary with the form of myocardial disease and with the individual condition. In the fat heart little can be expected from digitalis or strophanthus when the myocardium is already weak or there also exists arteriosclerosis. In the heart of Bright's disease when, notwithstanding the existence of heart disease, the blood-pressure goes down, caffein should be given in large doses and digitalis as well. In arteriosclerosis the blood pressure is an infallible guide to therapy; when it sinks the ordinary remedies should be applied; when it remains high it is not wise to give vasodilators. Myocardial disease due to other conditions, as chronic respiratory troubles, malformations of the thorax, etc., should be treated as all other chronic myocardial insufficiencies, in addition to which, at times, it may be possible to employ causal therapy.

Pericarditis does harm in two ways, either producing myocardial insufficiency by extension to the myocardium, by the production of adhesive processes or—which is rare—by the presence of fluid in the pericardial sac. When the latter exists the fluid should be removed; otherwise, the myocardial insufficiency should be treated.

Fourth and Sycamore Streets.

ABSTRACT OF DISCUSSION

Dr. De Lancey Rochester, Buffalo: I regret that Dr. Forchheimer could not go into the details regarding the treatment of dilatation of the right heart, because that is one of the conditions that it is not uncommon in pneumonia; in fact,

it is very common. It is one of the conditions in which venesection is particularly indicated. I can recall at present twelve cases of pneumonia with dilatation of the right heart, and in all of them I believe life was saved by doing a prompt venesection, withdrawing from 200 to 400 c.c. of blood. As illustrative of its value, I should like to report one case. This patient was 18 years old, and had had a progressive pneumonia involving one lobe after another, so that all the right lung and the upper lobe of the left as well as the pericardium were involved. The heart's apex was in the axillary line and the pulse was 180 or more, very irregular and small. The liver was two inches below the costal margin. There were present all the evidences of a dilated right heart. Flatness was complete on the right side, and it was feared that there might be fluid, and so the chest was aspirated in four directions, but nothing was found but solid lung. This patient was bled 250 c.c., and during the bleeding the respirations, which had been 66 to the minute, fell to 36; the pulse, which had been 180 and irregular and small, dropped to 120 and showed better tension. The heart, which had been in the axillary line moved to midway between the axillary and nipple lines in the fifth interspace and acted better. This patient's life was saved This illustrates one of the cases in which venesection was successful. It is a procedure which has gone into disrepute, but it should be used always when indicated.

DR. FRANK BILLINGS, Chicago: We all agree with Dr. Forchheimer that active measures are necessary when the cardiovascular syndrome develops; until that time, we are not all agreed as to what we should do with such patients. I think there is no disease in which rare judgment is so necessary not only in knowing what to give, but in knowing when not to give drugs. From my own experience I find that the longer I live and attempt to cure patients with pneumonia, the less I am inclined to give mixtures containing drugs until they are necessarily called for, and this is especially true in hospital work. The moment that cardiovascular symptoms appear, with the lowered blood pressure, with failing left heart, the time has then come for active work. I believe in the proper use of digitalis, but not as ordinarily given and by the mouth. With the hypodermic use of digitalis I have had a sad experience; it was with the active principles of the drug, and now I practically never use them. But I do use a preparation of the leaves themselves.

In an emergency, the intravenous use of digitalis gives good results. When used in that way it is not necessary to repeat the dose unless symptoms indicate. Four, six, ten, twelve doses may be necessary, and perhaps one dose, in some instances, will accomplish all that is necessary.

There are other remedies besides digitalis which increase the ordinary tone. Caffein is a good agent and camphor will

readily raise the blood-pressure in cases of failing left hearts. I give one or two-grain doses in ordinary camphorated oil. Musk also will raise the blood-pressure. Strychnin and other drugs that are commonly used in failing left heart are absolutely valueless except to stimulate nerve centers; strychnin will not raise the blood-pressure 1 mm. I have used it over and over again. If that unfortunate condition occurs, dilatation of the right heart, I think that venesection is the one remedy to be applied and immediately, and it matters not whether the patient be plethoric or not.

The use of cold applications to the chest I have followed. In failing heart the applications of bandages about the extremities is sometimes of value. But whatever is used must be used with good judgment or more harm than good may result.

Finally, the watchful and vigilant care of patients afflicted with pneumonia without the use of drugs is the ideal treatment. Do not attempt to do good by any specific medication, but attempt to preserve the functions of the individual's body, and do not be nihilistic regarding the use of remedies. I think we may say that with proper management of the patient we may occasionally save patients who might otherwise die.

Dr. C. F. Hoover, Cleveland: I wish to call attention to the danger of accepting a measurement of blood-pressure as an equivalent for the mass movement of blood. The fact that a patient has a maximum blood-pressure equal to a column of mercury 140 mm. high, does not justify the deduction that the mass movement of blood is satisfactory. Patients with severe mitral stenosis. for instance, may have a great disturbance in the blood distribution of the body with marked asystole, and still have a normal arterial pressure. The sphygmomanometer is not a safe guide in estimating the mass movement of blood. The position of the right border of cardiac dulness, the size of the liver, the pulsations in the internal jugular vein and the duration of the pulse in relation to the maximum systolic blood-pressure are all factors which must be considered in estimating circulatory efficiency. To estimate the size of the right auricle by percussion is one of the nicest refinements of physical diagnosis, and yet this very point is one which must be determined to settle the question of therapy in pneumonia if we are to anticipate an advanced cardiac incompetency with a suitable therapy.

Dr. John H. Musser, Philadelphia: It is very important that we should remember in those cases of apparent cardiac failure, that such cardiac failure is the result often of pericardial effusion. Too often do we see these patients treated for heart failure, or acute dilatation of the heart in the course of pneumonia when by removing a few ounces of fluid from the pericardial sac the serious symptoms are relieved.

Of course Dr. Forchheimer will agree that the best treatment of the heart is that which is applied in the first period of the disease, as soon as the pneumococcus infection is recognized. Therefore, the results that are to follow will depend on such form of management. I am in sympathy and in accord with what Dr. Billings stated. In the majority of the cases I prefer to rely on fresh air, on judicious local treatment, on hydrotherapeutics, on regulation of the proper amount of food taken, and particularly on care that the patient is not overfed. I watch carefully for the phenomena so well pictured by Dr. Forchheimer, guarding against the possibility of the vasomotor syndrome by proper renal elimination. Attention to proper elimination is of the greatest importance in the management of the cases of pneumonia, looking toward the prevention of cardiac failure; in other words, looking toward the reduction of serious toxic symptoms that arise and have expression more particularly in the phenomena just pointed out. To keep down the amount of food is of the greatest importance in the management of pneumonia patients. Watch carefully the state of the intestinal tract. Tympany is a serious toxic symptom in pneumonia and its increase with defective elimination is a point that I depend on as suggestive of the occurrence of vasomotor failure. This can be prevented very largely. Colitis occurs with the pneumococcus affection, and this colitis is undoubtedly the cause of the development of tympanitis; the colitis plus the toxemia invites an intestinal paresis. Hence to prevent this colitis which gives rise to the tympany, it is well to observe carefully the diet, regulating judiciously the amount and kind of food taken, and washing out the bowels with normal salt solution. Basing treatment on the idea that cardiac symptoms are threatened when renal insufficiency appears, I begin very early the use of caffein; this is perhaps the only remedy I would begin with as a routine measure. In addition I rely on cocain when the conditions become more extreme.

In regard to right-sided dilatation of the heart I agree with Dr. Rochester as to the value of early venesection. One must remember that we must not place too much stress on the physical signs brought out by percussion and auscultation. I am not so much disturbed by the development of murmurs suggestive of dilatation as I am of the appearance of vasomotor phenomena. I am not alarmed when asked to see cases of old valvulitis with mitral regurgitation. When we observe a murmur over the right heart, or a murmur at the apex, there comes into play the safety valve action of the tricuspid; this was pointed out long ago by Guiteras and often bodes much good in these cases.

Dr. Alexander Lambert, New York: Eight years ago I became dissatisfied with the results of the treatment of pneumonia that I had been following; they were very unsatisfac-

tory and I decided that when a large number of pneumonia cases came into the hospital, as at Bellevue Hospital, it would be well to compare the results of different treatments carried on simultaneously. In my division at Bellevue Hospital (there are four divisions), I gave up the use of alcohol and nitroglycerin and simply used those drugs by which we obtain a rise in blood-pressure. After three months, when each division had had from 125 to 137 patients each, I found that in those cases where alcohol and nitroglycerin has been used, the statistics were 10 per cent. higher in death rates in which the vasodilators had been used than were shown by those in which the drugs that raised the blood-pressure had been used. In other words, judging from about 500 patients affected with pneumonia, the death rate was improved 10 per cent. by camphor, caffein, digitalis and agents which raised the blood-pressure.

Dr. Theodore Potter, Indianapolis: The most remarkable phenomena occurring in lobar pneumonia are at the crisis and, in studying that crisis, it is made plain, as Dr. Forchheimer stated in his paper, that there is great danger to the heart, not from mechanical obstruction but from the toxemia. In dealing with this toxemia there are two chief things to help us; a rational comprehension of elimination in a natural way through the skin, kidneys and bowels, and an unlimited supply of fresh air to the lungs. After all, when these things are compared with drugs directed to the cardiovascular conditions, it seems to me they are far superior. Every one I think who has had to deal with pneumonia cases in an ordinary hospital has felt the great limitations under which he labors in the hospital ward. It is almost impossible in such hospitals to apply the rational fresh-air treatment in lobar pneumonia. Here, there are a large number of patients in the same ward; this is especially true in the large city hospitals. At times I have had to adopt certain expedients. I have taken patients into the delirium tremens room where the windows are kept open; here they could get the fresh-air treatment. But in private practice the problem confronts us, how to apply the fresh air treatment in a rational way. I am sure that everyone who sees such cases in his own practice or in consultation is confronted by it. I have got into the habit lately in teaching medical students of emphasizing the fact that the chief point in the whole matter of carrying out the fresh-air treatment, especially during the winter months it that there should be two rooms in the house for the treatment of such patients; that is practically the solution of the question. Time and again I have seen merely a crack of the window open; that is not real fresh-air treatment. The solution of this problem is in having a place for the patient and a place for the nurse. The nurse should have one room, and the patient another. This is the only way that the fresh-air treatment of these patients can be properly applied.

DR. FREDERICK FORCHHEIMER, Cincinnati: In making a diagnosis of congested or over-filled right heart, it is not necessary to prove by percussion, auscultation or inspection that the right heart is enlarged. The diagnosis of this condition can be made perfectly well by simply looking at the patient. It is almost impossible to err in regard to the existence of this form of heart trouble, or the existence of the Romberg-Pässler syndrome. In the Romberg-Pässler syndrome a vasomotor affection we have the addition of a profound anemia and a condition of collapse. In the other condition we find the opposite. We have fulness of the veins, congestion of the face, and all the evidence of dyspnea, an active dyspnea. There can be no mistake regarding the diagnosis, and one need not be so very particular about the direct examination of the right heart. In the treatment of this Romberg-Pässler syndrome, or vasomotor paralysis, I do not believe that digitalis is indicated, and for two reasons. In the first place it does not produce sufficient contraction of the splanchnic vessels to help in relieving the syndrome. In the second place if we increase the heart's activity by increasing the force of the systole, the result will be that the heart will force so much blood into the splanchnic area that it will be more embarrassed than before.

I do not believe we are going to gain much by the use of camphor, musk and other agents in this condition. I believe, however, that in cases of acute myocardial insufficiency either one of these remedies can be used with the greatest good to the patient. As to the question of blood pressure, I believe that Dr. Hoover is correct in what he has stated, but in conditions of splanchnic paralysis the blood-pressure tells the story; it shows that something extraordinary must have happened and this depends entirely on the localization of a mass of blood engorged in the splanchnic area. Those of us who have taken many blood-pressure observations have found that after the second or third day of a pneumonia the pressure is 100 or 102 mm.; that is a low pressure.

I have stated that, according to my belief, tympany is due to a vasomotor paralysis. That is why symptoms of tympany are always to be feared by the clinician.

We have all been using fresh air for a long time; in fact, v. Jürgensen recommended it in 1874 and possibly it was recommended even before that date. I have been using fresh air during the past thirty years in the treatment of pneumonia, and twenty-five years ago I published a paper on the subject. I think that of all the things recommended in the treatment of pneumonia fresh air is the most important. But there is no question regarding carrying out this plan of treatment in the hospitals; I think it can be carried out in the hospital even better than in private practice. All my patients in the hospital are treated by fresh air and simply by using a window tent or by keeping the windows wide open and the results are perfectly satisfactory.

I should like to make a statement in regard to the number of patients who have had this syndrome and whom I have treated. I have had a large number of such patients and I should say, without being mathematically correct, that about 50 per cent. were helped when the treatment was instituted early enough. Recently I saw a patient who had been suffering with this syndrome for twenty-four hours; I succeeded in raising the blood-pressure a little with adrenalin; the injection of caffein did not bring the blood-pressure up. A few hours later a second dose was given. I worked with that patient for some time but he finally died. If this patient had been treated early, and this is a very important part of the treatment, the result might have been different.

A CASE OF DIVERTICULUM AT THE PYLORUS

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History.—The case I have to report is that of a young man, aged 21, a college student in Toronto, who came to see me first on Sept. 22, 1894. His father and mother were living, the latter being of extremely nervous temperament and having had recurrent stomach trouble for some years. At the age of 18, the patient had experienced attacks of severe pain in the stomach after meals and when he saw me first, he complained of pain about two inches above the umbilicus, radiating a little to the left. There was no history of vomiting of blood. The thoracic organs were normal. He had a slight astigmatism with, at times, a trifling headache. He was cheerful and slept well. His appetite was very good and craving at times. His pain between meals was relieved by rest and milk and cream, egg or ice-cream. On examining his stomach, free hydrochloric acid was found present and after considerable retching there came through the stomach-tube a small quantity of blood-stained water and a fragment of mucous membrane, 1½ cm. long by 1 cm. wide which was soft and friabie and studded with dark extravasations, such as is sometimes found with gastric erosion or torn off by rough handling or suction of the stomach-tube. He was constipated; his urine was normal; he gave no specific history. There was no food stagnation. His symptoms abated and he improved on alkaline gastric sedatives with nux vomica, physostigma and stillingia. He came to see me again in 1905, four months after his appendix had been removed. He then complained of pain in his stomach which sometimes induced vomiting. The total acidity of his gastric contents was 60; free hydrochloric acid, 10 per cent. Acid salts, 12; combined chlorids, 20; biuret, present; rennet, present; erythrodextrin, +. Microscopic examination, negative. His stomach was empty before breakfast. Two days later, four and one-half hours after Riegel's test meal, there

was some mucus present; a total acidity of 30; free hydrochloric acid, 0.09 per cent. He returned home and on rest, fresh air and tonics, improved very much. In September, 1906, he came back complaining of vomiting and gastric pain, flatulency and loss of weight. Again in May, 1908, shortly after returning from England, he came with gastric symptoms similar to those he had presented in the past.

Operation.—Dr. Cornell, of Brockville, Ontario, being present and concurring, on Nov. 25, 1908, Dr. Carlton C. Frederick operated and reports the following: There were adhesions found about 2 cm. in diameter, about 4 cm. from the pylorus on the anterior stomach wall, between it and the transverse colon and gastrocolic omentum. The adhesions were broken up and the denuded surface closed over by fresh peritoneum. Between this point of adhesion and the pylorus, just inside the pyloric ring on the stomach side, was a diverticulum consisting, apparently, of serous and mucus membranes only. To remove this diverticulum necessitated doing a modified Finney operation. The modification consisted in bringing the duodenum farther forward than in the ordinary operation for pyloroplasty, and after the first line of sutures, which are usually passed through the peritoneum, instead of making the horseshoe-shaped incision the diverticulum was excised, and from its upper curve the balance of the necessary horseshoe-shaped incision was carried beyond the pylorus down to a sufficient distance in the duodenum. After the operation was completed, the duodenum lay in front of the anterior wall of the pyloric end of the stomach instead of in the usual position after a Finney operation, along the subpyloric curve.

Postoperative History.—Since the operation the patient has gradually improved and now weighs 136 pounds. When he left the hospital his weight was 104. He makes no complaint of his stomach and says he feels better than he ever did.

The interesting points about this case are, first, that it is probable that the patient had a gastric ulcer at the age of 18; that this ulcer destroyed the muscular coat of the stomach, and that in healing this coat was not restored, but the pyloric wall in that region consisted chiefly of the serous and mucous coats, the latter having undergone regeneration. This thin and weak portion of the pylorus gradually stretched and formed a diverticulum. As a rule, gastric ulcer at or near the pylorus gives rise to cicatricial contraction, with more or less stenosis following, but in this instance such was not the case.

The second point of interest simply consists in the illustration that this case affords of the fact that cases of long-standing gastric complaint often show organic disease of the stomach or adnexæ. The examination of the gastric contents showed a variable chemistry in this case, and revealed also an unstable motor condition.

During the years between 1893 and 1908 the patient was a gastric semi-invalid, and his tolerance of the organic change in and near his pylorus was insufficient to maintain him in vigorous resistance and health, probably owing to his temperament and a delicate physique. His gastric symptoms consisted usually of a combination often present in gastric neuroses, which emphasizes once more the clinical fact that some or all of the symptoms of the gastric neuroses may exist with structural alteration and that operation, which should have been done earlier in this case, affords the only relief or cure for such structural change.

In the causation of this patient's symptoms, the perigastric adhesions may have been chiefly instrumental, although it is impossible to estimate the degree of disturbance caused by the deformity of the pylorus, the caliber of which was ample.

436 Franklin Street.

ABSTRACT OF DISCUSSION

DR. CHARLES G. STOCKTON, Buffalo: This seems to me to be a very unusual case. So far as I know, this is the only instance in which a diverticulum has appeared in that region and the only instance that I know of what undoubtedly was a gastric ulcer so destroying the wall of the stomach as to result in a diverticulum. Those two facts appeared undoubtedly in the case reported by Dr. Jones.

DR. ALLEN A. JONES, Buffalo: This diverticulum was two and a half centimeters (2.5 cm.) in depth. It had pressed on and dilated the pyloric ring, really involving a part of it. It also dilated the duodenum two centimeters (2 cm.) beyond the ring. With this pressure in the antrum pylori one can readily understand how it would become a condition that would be a symptom producer. It is impossible for us to say now how much perigastric adhesions had to do with the causation of the symptoms, or how much the deformed condition of the pylorus was to blame.

BACTERIAL EXAMINATION OF THE STOOLS IN SUSPECTED CANCER OF THE STOMACH

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It is surprising that the facts presented by Rudolf Schmidt from Neusser's clinic in 1906 regarding the presence of the Boas-Oppler bacilli in the stools in cancer of the stomach has attracted so little attention in view both of Schmidt's well-known standing and the expressed conviction of Neusser as to the significance of the finding. Schmidt showed the following fact: The bacterial examination of the stools by Gram's stain under normal conditions gave a picture of very few organisms, the Gram-negative colon group vastly outnumbering any Gram-positive organisms. The normal stool Schmidt called Gram-negative. A stool that with Gram's method showed uniform-sized bacilli far outnumbering all other organisms he regarded as Gram-positive. Occasionally a stool was found in which Gram-staining organisms in great varieties outnumbered other organisms; these organisms were chiefly cocci and non-uniform bacilli which he differentiated in a manner to be referred to later. They are not Gram-positive in the sense that the predominating organism is a well-staining uniform bacillus. Schmidt takes the ground that Boas-Oppler bacilli are vastly more easily found in the stools than in the gastric contents, which is quite true, and he believes that if the morphologic characteristics of the Boas-Oppler bacilli are determined in differentiating them, their relation to cancer becomes of greater

significance. He has stated, as have a great many other observers who have followed the matter carefully, that many organisms have been mistaken for the Boas-Oppler bacilli. This has served to put the relation of the Boas-Oppler organism to cancer in considerable doubt. While not contending that the occurrence of the organism is characteristic of cancer, Schmidt points out how easily the organism is mistaken for certain other bacilli. Every one who has studied this question at all will admit at once that our diagnosis of Boas-Oppler bacilli is made on very insufficient grounds, when one considers the care that Schmidt has exercised in differentiating them. Certainly hereafter all the deductions about the relation of the organism to cancer must be made on an absolute determination of what is the Boas-Oppler bacillus.

In a study of a large series of cases from Neusser's clinic and from the subsequent reports by a few other observers, the following deductions may be made:

1. A typical Gram-positive stool may occur in:
   Primary cancer of stomach.
   Ulcer of stomach (Elliott. Not confirmed at operation or autopsy).
   Typhoid (Neusser).
   Cancer of the uterus with emaciation and cachexia (Neusser).
2. "Gram-negative stools exclude cancer of the stomach" (Neusser).

Elliott, however, found a secondary cancer of the splenic region with a Gram-negative stool, and one other gastric cancer with uremia and excessive vomiting, also with a Gram-negative stool.

My own findings thus far in a series of cases of cancer of the stomach in which the diagnosis was confirmed at operation or autopsy have failed to show any cases in which the stool was other than Gram-positive, and in no case of acute or chronic ulcer has the stool been other than Gram-negative, on repeated examinations.

The most interest, however, centers about four cases in which a diagnosis of gastric ulcer was made on ac-

count of the clinical history, pain, lack of cachexia and the presence of free hydrochloric acid in the stomach. Although the bacteriologic examination of the stool had been made in each case, its importance was not held to be sufficient to warrant its being weighed in the evidence. In each case an operation was performed and the diagnosis made clinically as follows:

CASE 1.—Clinical diagnosis, ulcer of stomach at pylorus. Operation, extirpation of pylorus. Microscopic examination: diagnosis, malignant degeneration of ulcer in the pyloric opening.

CASE 2.—Clinical diagnosis, ulcer of stomach. Operation, gastroenterostomy. Death from hemorrhage. Diagnosis at autopsy, malignant degeneration of ulcer of the lesser curvature near pylorus.

CASE 3.—Clinical diagnosis of multiple ulcer with uncontrollable hemorrhage. Operation, gastroenterostomy; revealed extensive secondary cancer, a primary tumor in the gall- bladder, stomach wall involved in several places. Diagnosis confirmed at autopsy.

CASE 4.—Clinical diagnosis of ulcer of the pylorus. Operation, pylorectomy. Several areas of cancerous degeneration in large ulcer at pylorus.

I have not entered into detail in these cases as to the ground for clinical diagnosis of ulcer of the stomach. I believe in each case that such a diagnosis was entirely justifiable in the light of the symptoms. The significant point of it is the great importance that was apparently attached to the one symptom that was not weighed with the others. Personally, I should continue the bacteriologic examination of the stools in doubtful cases with very much more interest than before, for not only is the early diagnosis of cancer a matter of the utmost importance, but one can not fail to be impressed with the extraordinary reports of the Mayos as to the frequency with which cancerous degeneration of ulcer occurs.

Schmidt's technic is as follows:

Make thin smears.

Dry and fix five minutes in methyl alcohol (thus dissolving also fat).

Stain five minutes in anilin-oil-gentian-violet; wash.

Iodin-potassium-iodid solution till deep purple; wash.

Decolorize in 95 per cent. alcohol till nearly colorless; wash.

Stain in weak aqueous solution of fuchsin; wash; dry; mount.

In considering the difficulties in recognizing the Boas-Oppler bacilli, Schmidt calls attention to the following types:

1. Lactic acid bacillus type; these organisms are thinner than the colon group, vary greatly in length, show no spore formation, are non-motile, show areas of Gram-negative stain, stain yellow with Lugol solution and show granules in the protoplasm. All characteristics are identical with the bacilli found in the coffee-ground vomitus of cancer of the stomach.

2. Pseudo-colon group; these have the same morphology as the Gram-negative colon group, except that they are Gram-positive and non-cultivable. They occur in catarrh of the bowel, especially with acid stools.

3. Gram-positive bacilli, thicker than the Boas-Oppler and occurring in long chains, staining blue with Lugol solution, non-cultivable; occurring in chronic catarrh of the lower bowel, especially when atony and flatulence are present.

4. Emerson says that "some passing under this name (i. e., Boas-Oppler), are surely the gas bacillus."

5. It seems probable that the common *bacillus subtilis* is often mistaken for the Boas-Oppler, especially in stained specimens of stomach contents.

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ABSTRACT OF DISCUSSION

DR. HERMAN B. ALLYN, Philadelphia: Do the bacilli which are Gram-positive appear early in the stools in cancer of the stomach?

DR. ALLEN A. JONES, Buffalo: Has Dr. Brown found the Oppler-Boas bacilli in the gastric contents in those cases in which the bacilli were Gram-positive in the stools? If so, did the cases prove later to be gastric cancer?

DR. ANTHONY BASSLER, New York: I have also observed the Boas-Oppler bacilli in the stools in some instances of gastric carcinoma. Recently I have been interested in making slides from the back of the tongue and throat in stomach cases. While in vomiting they are often found in the mouth, lately I saw

a case in which there was no vomiting, but the organisms were found in large numbers, probably having been carried up by the eructations that were present.

DR. PHILIP KING BROWN, San Francisco: I found these bacilli in the stools early in cases of cancer. In four cases in particular in which diagnosis of ulcer was considered the most probable one, they were evident. If these bacilli are Gram-positive, they should make one suspicious of cancer of the stomach. I did not look for them in the gastric contents. In the four cases attended with Gram-positive findings, the diagnosis was confirmed finally at autopsy or at operation.

AMEBIC DYSENTERY

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Dysentery has been known as an independent malady of widespread and almost universal distribution since the most remote period of time. In the very earliest writings on medicine references may be found to the disease, and the part it has played through the ages, especially in connection with the fatalities of army life, has left an impress on the historical records of nearly every nation. It is only within what might be called modern times, however, that a step has been made toward the closer analysis and classification of the disease. The differentiation of the old-time bloody flux, with its confused clinical picture, into the two clearly defined types identified to-day under the names of amebic and bacillary dysentery, has been the result of investigations entered upon only within the past half-century.

HISTORY

Lambl, in 1859, was in fact the first to offer the suggestion of a possible specific cause for dysentery. In the course of a routine examination of the intestinal mucus of a child who had died of enteritis he ran across an ameboid body, probably a flagellate, which impressed him as a possible factor in the inflammatory process. This observation did not, however, seem to create much comment at the time and no further investigation was made in this direction until 1875, when Loesch was

able to identify probably the first true amebæ in the dejecta of a characteristic case of dysentery, originating in St. Petersburg. Eleven years later Kartulis, working in Egypt, always a hotbed of dysentery, reported 150 cases from that country, in all of which he found the ameba. Subsequently he noted the same organism in liver abscesses. Koch had, however, three years before, demonstrated amebæ in sections from an ulcerated bowel, showing a direct causal relationship between the parasite and the intestinal lesion.

In this country the first amebæ discovered were by Osler, in 1890. Shortly afterward, confirmation came from various sources. Within one year Stengel found 3 cases of true amebic dysentery in Philadelphia and Musser 4 from the same city, while Dock was able to report 12 cases of the acute and chronic types from Galveston, the first to be recorded from the far South. The disease has subsequently been found to exist, scattered over many other sections of this country, and, in fact, in nearly all parts of the world sporadic cases crop out occasionally, apparently of purely indigenous origin. Even in such northern latitudes as Germany, England, Japan, or even Russia, there come reports at times of its occurrence; but the disease is essentially a tropical or semitropical one and prevails more extensively in warm climates, in connection usually with a low-lying or poorly drained soil.

In certain regions of the South, including a comparatively large area of our country, conditions are almost ideal for the prevalence of an amebic infection. It is only within very recent years, however, that its occurrence in the South, in wide-spread endemic form, has come to be suspected, and even to-day the question is scarcely regarded by the profession in a light at all befitting its high importance. In spite of the frequent case-reports from Southern observers, the impression has nevertheless seemed to persist in part that the disease is of rare occurrence in the United States and that

the relatively few instances which find their way into print might be traced to a previous residence in the tropics. This impression should no longer be allowed to go unchallenged. As far at least as the South is concerned nothing could be falser. The disease, it should be insisted on with the greatest possible emphasis, does find a home ideal for its existence and dissemination in the semitropical environment of the South, is and has been for years widely prevalent there, though unfortunately masked all too frequently under the vague and generalized term of simple chronic diarrhea, or some such indefinite diagnosis.

Of the truth of these facts there can be found testimony sufficiently suggestive in the various scattered case reports of Southern observers, such as Harris from Atlanta, Jelks from Memphis, Wilson from Birmingham, Wasdin from Charleston, Dock from Galveston, Slaughter from Virginia, and many others. As a further contribution to this array of evidence I wish to offer an additional group of 50 cases from New Orleans, which I have been able to collect during the past two years, partly from my own records and partly from those of my colleagues with whom I am associated in the hospitals. These few cases. I need only remark, serve merely an an index to the prevalence of the amebic dysentery in our particular section and do not in any way begin to cover the field. On the contrary, I am convinced that, were the full facts known, as they should be, the number of cases at present unrecognized and overlooked in all parts of the South would be found to foot into the many hundreds. In fact, the tardy recognition accorded this wide-spread amebic infection bears a faint resemblance to the history of the hookworm disease in the South. Before Stiles' epoch-making discovery, thousands of hookworm sufferers, as we now know, dragged out a miserable existence, weighted down in most instances under a false diagnosis.

In part extenuation of this hesitancy and failure in recognition, the extremely variable and capricious symptom picture of amebic dysentery, it is true, makes a purely bedside diagnosis uncertain, and may even tend to disarm an ordinary suspicion of its existence. The term "dysentery" has come to be associated in our minds with such classical symptoms as an outspoken tenesmus, small, frequent and liquid evacuation, containing blood and mucus, all running a more or less rapid and acute course. This clinical picture, however, could scarcely be used as a descriptive one for the so-called dysentery of amebic origin. In the first place, this condition is practically always chronic, in the sense of a protracted infection, and the acute types occasionally met may be looked on as mere exacerbations. The number of years the infection might exist in latent form, or, if established, remain unrecognized, is very variable and depends largely on the ability of the physician in making the diagnosis.

Among my series of 50 cases, in one the disease could be traced back twelve years, in another eight years, in 2 instances six years, and in 5 cases the condition had been present two years at the time of the first consultation. The average duration of the cases was about nine months.

The symptoms of amebic dysentery, as I have said, are not always clearly defined and constant. During its course there are quiescent periods, when apparently all trace of the trouble has vanished. The bowels might even become obstinately constipated. The amebæ remain, however, constantly under cover during this time, the infection suddenly flaring out again under conditions favoring renewed activity. These occasional attacks of diarrhea, alternating with periods of normal evacuations or constipation, make up a very suggestive picture of an amebiasis, and when present should lead to an immediate examination of the stools for the amebæ.

When attacks of diarrhea do occur, the number and character of the evacuations do not follow any set rule. A great deal depends on the location of the ulcers. If low down, and especially if in the rectum, the evacuations are usually frequent and a marked tenesmus, with soreness of the lower bowel, is noted. If the main lesions are above the sigmoid, as they most frequently are, the number of stools may never average above two to three per day. Mucus may or may not be present, but commonly is. Pure blood, or a blood-streaked mucus, I have found to be fairly constant, though at times in only small amounts. In one of my fatal cases, with liver abscess as a complication, the patient suffered severe hemorrhages, a symptom which, according to Strong, is always suggestive of abscess.

As far as the influence of age is concerned, the average in my cases was 37 years. This is in line with the usual figures given. The oldest of my patients was 60 and the youngest 22. The disease is rare among children, the dysenteric infections in early life being mostly of the bacillary type.

The colored race does not figure largely in my series, in which there were 42 whites and only 8 negroes. This, from a Southern city, in a non-selected field, is suggestive, as showing the relative infrequency of the disease among the blacks. Again, only 6 of the 50 patients were females, thus exhibiting a large preponderance of males affected. Occupation and the greater exposure of males to infection in general would, I believe, sufficiently explain this difference. Among my cases 25 were common laborers, 3 were farmers, 4 merchants, 2 bakers and 1 was a rabbi.

In the determination of the prevalence and endemicity of the disease in a particular locality, the nativity and immediate residence of the patients become of importance. Fifty per cent. of the patients I observed were born in Louisiana and had never lived in any other state or country, while an additional 14 per cent. had resided

in Louisiana five years prior to the onset of the disease. In only two instances could the infection be traced definitely to the tropics. The remainder all came from neighboring Southern states. These figures, I believe, require no further comment in refutation of the views sometimes held that amebic dysentery rarely originates in this country and—more especially to the point—in the South.

The prognosis and, in a sense, the curability of this, as of other diseases, is largely determined by the period of its recognition. In a general way it may be said that the longer the infection has continued the greater probability there is of serious complication. Seventeen, or 28 per cent., of the fifty patients whose cases I have tabulated died. In 15 of these the cause of death was determined accurately by post-mortem. Extensive ulceration of the large bowel was found in practically all, but in nine instances this was found to be the sole cause of the fatal termination. Perforation was observed in but one case.

Six cases of abscess of the liver were recorded in these autopsy records, 5 solitary and 1 multiple. This complication is always an important and serious one. Figures differ, however, as to its frequency. In Futcher's cases, liver abscess was diagnosed in 22 per cent., in Craig's 33 per cent., and in Harris' only 15 per cent. All agree as to the infrequency of this condition in the female sex. All my patients were males. There is one point in connection with amebic liver abscess which I believe should be emphasized. The condition is looked for in the amebic infected districts all too rarely. The diagnostic puncture of the liver is always a simple procedure and is attended with practically no danger. Since the symptoms of an abscess are often so uncertain, the use of the aspirator is indicated when the merest grounds for suspicion are present. Only thus may a serious and often irretrievable oversight be avoided.

When we step now from the discussion of the purely clinical aspect of the amebic infections to a consideration of the organism itself, another chapter of almost equal importance spreads itself before us. The studies of recent years into the biologic and morphologic properties of the ameba have had, in fact, a highly important bearing on the solution of many of the hitherto vexed problems of the disease. Of these problems the principal have hinged on the question of the actual pathogenicity of the ameba to man, as well as on the separation, if such were possible, of a harmless from a disease-producing variety. It has been the lack of just such a differentiation in the past which has occasioned the degree of confusion in diagnosis and brought about the frequent false and contradictory reports in regard to the treatment. The earlier investigators recognized but one type of parasite, which, because of its connection with colonic infection, accidental or otherwise, they termed *Amœba coli* (Loesch). In 1891 Councilman and Lafleur, in their splendid studies, proposed that this name be dropped and that of *Amœba dysenteriæ* be substituted, since they believed that they had established a definite causal relationship between the ameba and the dysenteric lesions. They also hinted at the possibility of a non-pathogenic organism, for which the old term *Amœba coli,* they thought, might hold. Subsequently, several other forms of nomenclature were suggested, but it remained for Schaudinn, in 1903, following closely upon Jurgen's work, to announce the first definite and scientific classification of the amebæ. He retained the term *Entamœba,* previously suggested by Casigrandi, as the proper designation for the particular genus invading the intestine, but drew a sharp line of distinction between a type found pathogenic to man and cats, which he named *Entamœba histolytica* and a non-pathogenic, which he termed *Entamœba coli.*

Schaudinn's classification and conclusions have now been fully confirmed by the majority of competent ob-

servers, with the notable exception of Musgrave and Clegg, who still maintain that there is insufficient grounds for such a differentiation. The more recent, exhaustive studies of Craig, Viereck, Flexner and others leave little justification, however, for further doubt.

The two forms have many points of difference, both structural and bionomic, which allows of an easy differentiation between them.

This holds for native as well as stained preparations. I have found the Wright stain, as recommended by Craig, satisfactory.

Now that pure cultures of the *Entamœba histolytica* in guinea-pig serum has been found possible without symbiosis, a further insight into the life-history of this organism and its behavior under various conditions might be hoped for.

The question of the distribution of the *Entamœba coli* over the various regions of the world, as well as the proportion of healthy individuals infected with this apparently harmless parasite, are points which in part still remain open for further investigation and study. According to Craig, 71 per cent. of healthy individuals in the Philippines are found to harbor this organism, while the stools of 65 per cent. of the active soldiers stationed in San Francisco were likewise found infected. Schaudinn's figures, along the same line, average 50 per cent. for West Prussia, 20 per cent. for Berlin and 66 per cent. for those examined in the neighborhood of the Adriatic Sea. Dock, however, examined 200 normal subjects in Michigan and found the *Entamœba coli* in but two, or 1 per cent., of the whole. My own experiences in New Orleans, while not as yet based on a large or systematic scale in this field have indicated at least the relative infrequency of the *Entamœba coli* in Louisiana. The association of the harmless with the pathogenic type seems to be the rule in the Philippines; but I am yet to see an instance of this in our section.

In a large proportion of the stools I examined, however, *Cercomonas hominis* were found and in five of my cases I noted the *Strongyloides stercoralis* in connection with the *Entamœba histolytica.* Noc has recently called attention to this point and asserts that the so-called Cochin-China diarrhea, which was formerly thought to be solely due to a strongyloides infection, is in reality amebic dysentery, which in China is frequently complicated by the presence of the strongyloides worm.

TREATMENT

While substantial progress has been made, as we have seen, during the past half-century in almost every department of the subject of amebic dysentery, the matter of treatment still remains in almost as unsettled and undetermined state as before. There appears to be little chance, even to-day, with our advanced conceptions of the many phases of the disease and its problems for any unity of opinion as to the proper methods of its control. In the past, empiricism has been the sole guide and unfortunately holds sway to a great extent down to the present time. Every clinician would seem to hold individual ideas of the proper methods of treatment and those, too, largely irrespective of the experiences of others.

For hundreds of years ipecacuanha has been held in the highest esteem, above all other remedies, in East India and neighboring Oriental countries. This drug thus has at least the authority of longest usage and even to-day is regarded in Indian practice as almost a *sine qua non* in the treatment of amebic dysentery. Contrasted with this experience, however, there is a mass of contradictory testimony from other sources in which ipecac has seemingly been found totally inadequate. The experience of our army officers in the Philippines, for example, has always appeared particularly unfavorable to the use of ipecac. Strong, in his recent article in "Modern Medicine," discusses the ipecac treatment

with a bare word, stating that the drug is "in no sense curative." Jackson is even more outspoken in his opposition. He says, in regard to this remedy, that he "has seen it thoroughly tried and is convinced of its utter uselessness and also of its harmfulness." From other countries, equally unfavorable experiences are recorded from time to time in the literature. Manson, however, always a great enthusiast in regard to the ipecac treatment, in his latest utterances on the subject, again puts forth a plea with his brethren in other lands, for another trial of this drug. Impressed with the weight of such high authority, and especially when born of so large an experience, I have ventured to employ ipecac in my cases during the past two years and am ready to acknowledge now my thorough conversion to the sanguine views of Manson and other English authorities in the tropics.

The detailed method of its administration is, I believe, of the greatest importance, the lack of which stands as explanation in part for the failures reported in some quarters. First of all, the drug should be administered only in pill form, coated to the extent of about an eighth of an inch with phenyl salicylate (salol). The patient must be put to bed for the first two weeks' treatment and his diet restricted to liquids or, at most, light solids. This absolute rest in bed, with restricted diet, is particularly essential to the details of the plan. Castor-oil may be given as an initial purgative and then each evening, after a three hours' fast, the pills coated with phenyl salicylate are administered. A start may be made with 40 or 60 grains, depending on the length or severity of the infection, but each subsequent evening the dose is reduced 5 grains, until the limit of 10 grains is reached. Following this, I have been in the habit of continuing with 10 grains each day for the next two weeks.

The use of the drug in this way has appeared to me almost in the light of a specific. Under its influence

the stools become diarrheic, soft and pultaceous and the amebas seem to vanish almost at once, even though careful search be made for them. Opium is no longer required to prevent nausea or vomiting, if ordinary care be taken to have the pills well coated with phenyl salicylate.

The *modus operandi* of ipecac, which might account for the success following its administration, has never been satisfactorily explained. There is certainly nothing in the known physiologic effects of the drug which would suggest an explanation of its efficiency in this particular field. It seems plausible to infer, however, that ipecacuanha principles, through some intestinal changes, become inimical to the life of the amebas.

Bowel flushes, on which almost exclusive reliance is placed in some quarters, may or may not be employed in connection with the ipecac treatment. I prefer to make use of irrigations, however, principally as a means of washing away débris from the ulcerated bowel and begin with this procedure usually after the ipecac has been brought down to the limit of 10 grains per day. The character of the solution is not of great importance, so long as a sufficient quantity of water for thorough cleansing of the bowel is employed. Before my success with ipecac I had found all forms of solutions unsatisfactory. I believe simple saline solution fulfills the full requirements as a bland non-irritant bowel wash. As an after-treatment, nitrate of silver solutions may be indicated as a curative agent for the still remaining ulcerations.

What shall be said, finally, in regard to surgical intervention in intractable forms of the disease? The comparatively simple operation of appendicostomy, which, if properly performed, it is asserted, will permit a more satisfactory flushing of the large bowel, has found many advocates in this country in recent years. Its rationale, however, is not quite as clear as some enthusiasts of the

plan would have us believe, and it is wise that the whole question be allowed to remain open for more extended trial and investigation.

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ABSTRACT OF DISCUSSION

DR. THOMAS B. FUTCHER, Baltimore: In 1903, at the New Orleans Session of the American Medical Association, I analyzed our experience at the Johns Hopkins Hospital with cases of this disease during fourteen years, since the hospital was opened. At that time, there had been 119 cases of amebic dysentery in the wards. It was interesting to note that being not far north of the Mason and Dixon line, 95 of the 119 patients had never been out of the state of Maryland, and that the infection, therefore, must have been contracted there. The most important complication of the disease, of course, is amebic abscess of the liver. Among the 119 cases there were 27, or 22.6 per cent., amebic abscesses; 9 of these abscesses ruptured into the lung causing pulmonary abscess. One of these subsequently ruptured into the pleural sac, producing a pyopneumothorax; 3 of them had empyema. In 3 of the liver abscess cases the inferior vena cava was invaded. One case had a remarkable result; the abscess ruptured into the vena cava and there occurred a thrombus extending into the right auricle. This case has already been reported by Dr. Flexner. It is surprising, when we consider the extent and depth of the ulcers in this disease, that there are not more intestinal hemorrhages than do occur. There were but three instances of severe hemorrhage in our series of cases; all these had a fatal termination. There were 3 cases of perforation of the bowel, with a resulting peritonitis. One was recognized early and the patient was operated on, but died. There was one case in the wards in which an abscess was found in the floor of the mouth. The pus from the abscess contained ameba. This case has also been reported by Dr. Flexner. I wish to emphasize Dr. Simon's statement regarding the prevalence of the disease; I believe that it is of more frequent occurrence than is supposed. This disease can only be recognized by a most careful and systematic examination of the stools. There was one patient who came into the wards at Johns Hopkins four years ago suffering from diarrhea, in whom examinations of the stools gave negative results. Recently he again returned to the hospital and amebas were found in the stools. I have no doubt but that four years ago he had amebic dysentery. A careful and systematic examination of the stools should always be made, not once, but repeatedly. With reference to the operation of appendicostomy, that is, suturing the amputated appendix in the abdominal wound and irrigating the colon through this fistula, I would say that the results with us, so

far, have been unsatisfactory, although our experience is limited. One man had appendicostomy performed Sept. 9, 1907; until April 14 of the following year, 1908, he had had daily irrigations of quinin solution, 1 to 500, and occasionally of nitrate of silver solutions, and of peroxid of hydrogen, etc. Only one month before he left the hospital did the amebas disappear from the stools. I have not been able to follow him since. This was certainly not a satisfactory result. There have been two other cases in the hospital in which appendicostomy has been performed without having given what we consider satisfactory results. Since Dr. Dock reported at this year's meeting of the Association of Tropical Medicine in Washington the results of the use of ipecac, Dr. Barker has employed it in two cases in his wards. Dr. Boggs told me yesterday that after the first dose a most thorough examination of the stools failed to reveal amebas. This is a remarkable result. I feel that the ipecac treatment ought to be given a thorough trial, so that we can see whether the results obtained are more satisfactory than are gotten by other methods. The ipecac is given in salol-covered pills, 20 grains to the dose, three times a day. Dr. Dock states that it may be given in smaller doses at shorter intervals, aggregating from 60 to 80 grains in twenty-four hours.

Dr. George Dock, New Orleans: The importance of the subject that Dr. Simon has brought up is realized by everybody who comes in contact with cases of chronic diarrhea. The geographical distribution of dysentery is certainly great; south of the latitude of Louisville, Ky., it is a very common disease. I reported a case occurring in the lower portion of Michigan in 1902. After that I discovered another case in northern Michigan; this patient had never been out of the county in which he lived. So the disease should be looked for wherever there is any chronic disturbance of the intestines. It is important for us to remember that a patient with chronic dysentery, true amebic dysentery, does not have the classical symptoms of dysentery all the time. The stools may appear normal for long periods of time. I should like to speak of some of the practical details in examining the stools of these patients. Ordinarily, it is easy to have a patient pass a stool at command. An examination of a stool with the naked eye is often unsatisfactory. Even an examination by the microscope may be negative. Therefore, in a negative case we should never be satisfied with a single examination or even with repeated examinations of ordinary stools. The next thing to do is to examine by rectum with a tube or speculum. It is better to pass the tube or speculum into the rectum; to use no grease on it, because it interferes with the examination. By working the instrument around, it will enter and sometimes we can get very positive information. If this examination should be negative, I think it is essential to give the patient a dose of salts, say Carlsbad salts, in order to

produce watery stools. It is easy to understand by an examination of the intestine how a stool can be passed without amebas with it. The amebas lie in the abscesses or in the ulcers along the wall of the intestines and the stool passes by without mixing them in. I recall an interesting and instructive experience I had with a case that was diagnosed as amebic dysentery from the symptoms, yet was unable to find the amebas when the patient had a natural stool. A rectal tube was passed, but the patient complained so that it had to be removed. I then passed my finger into the rectum and got a lot of stuff which was filled with amebas. Why they were not forced out before I could only surmise. In the examination of the material it is not necessary to use a warm stage. Even in fairly cool weather the amebas keep up their activity for sometimes three or four hours. It is better, however, to examine them fresh; it is easier to detect them when they are lively. There is another point which I think should be mentioned. Beginners are easily led astray by the presence of large cells which they think are amebas. Red cells may be included in them. I have found people who had great difficulty in differentiating them.

I am glad that the success with the ipecac treatment has been confirmed by the results obtained in Dr. Barker's two cases. When we speak of results I must admit that many of the patients could not be followed up; so we could not be certain that they were entirely cured. Some patients have come back with the disease after weeks or months, four or five months, and we have not been able to find amebas, either with the aid of the rectal tube or speculum, or with the use of the Carlsbad salts. I recall the case of a man with the disease; he came from the Philippines and had been under treatment for two years; he had been given quinin, salicylic acid, etc. This patient was readily cured by the use of ipecac according to the method of Roberts. He was given 7 grams, or 105 grains, of ipecac in pills covered with salol. The amebas immediately disappeared from his stools. When he left the hospital I thought he might have a recurrence. He wrote me four years later and stated that he had "consumption." I supposed the amebic dysentery had returned with abscess of the liver, and I asked him to come back for examination. He returned and I found that he had tuberculosis. A very thorough examination of the stools failed to reveal any amebas. There were no signs of liver abscess. The failure of the operation of appendicostomy is what we should expect in some cases. The attempt to irrigate the colon through the cecum, washing downward, must fail in washing out the tube thoroughly. At all events, it would be well to try ipecac before resorting to an operation.

DR. HOBART A. HARE, Philadelphia: I think that much interest in this discussion lies in the fact that thirty years ago Stille taught his students to use ipecac at a time when they

had no conception that amebas produced the disease. In May, I received a paper from Dr. Rogers of the Indian Medical Service practically repeating the facts already published in regard to the value of ipecac not only for the cure of dysentery but as a prophylactic against amebic abscess of the liver. The claims he makes for the prevention of hepatic complications by the employment of ipecac are so strong that, if his results are proved to be correct, the use of this agent should be resorted to in every case of amebic dysentery. The instances in which appendicostomy has proved of value constitute a class by themselves, a class in which the appendix acts as a focus of infection for the bowel. The cure does not follow from the irrigation used in the colon, but because it removes the focus of infection in the appendix. In a number of cases of so-called mucomembranous enteritis or colitis which seemed to be associated with neurasthenic conditions, I have seen the removal of the appendix result in a cure, simply because when the appendix was opened it was found to contain one or two drops of pus, and I have seen the physician in attendance disappointed because he thought the operation was going to be a failure so far as an ultimate cure was concerned, when in reality the removal of the infecting focus was exactly what was needed. And so in amebic cases, the appendix oozes out infection day by day. I am glad Dr. Dock spoke of the difficulty of irrigating the colon through the appendix; I am inclined to believe that this is no safe procedure. Some may remember that about twenty years ago experiments were made to determine just how much pressure the intestine could stand. It was proved that a pressure greater than that exercised by a fountain syringe placed twenty inches above the table was dangerous. This is the pressure we ordinarily get. This is more dangerous in a diseased gut, particularly when the lesions are ulcers the result of amebic infection. I agree that it is necessary to have proper technic in the use of ipecac. If not given properly it fails. Three or four surgeons returning to the United States from tropical countries have told me that this treatment only failed when the method of administration was erroneous. A very interesting point concerns the geographical distribution of the disease. Jefferson College Hospital is one of the largest in the country, more than 5,400 patients being admitted to the wards annually. There is a correspondingly large outdoor service. I have charge of these wards six months out of every year. I think I can remember but three cases of amebic dysentery occurring in the eighteen years that I have had charge of this service. We have a different service from that at the Johns Hopkins Hospital not only as regards dysentery, but as regards malaria, and yet we are only distant about one hundred miles. This difference is extraordinary. I am sure that the same conditions exist in other Philadelphia hospitals.

DR. HUGO A. FREUND, Detroit, Mich.: I can bear witness to Dr. Simon's statement about the widespread prevalence of dysentery. The cases are not necessarily endemic for it seems to me that they are coming from different portions of the globe. Last year I treated two cases of amebic dysentery that in some ways were of great interest. At the suggestion of Dr. Dock the first patient was treated with the salol-covered ipecac pills, 5 grains being given at a dose, and repeated every hour. But my method of administration differed somewhat from his. I first prepared the patient for medication. The first time the ipecac was given, 65 grains altogether, there was considerable diarrhea, tenesmus and pain. An examination of the stools the next morning, to my astonishment, revealed no amebas, nor could any forms resembling dead ones be found. For the next two weeks I gave the patient nothing but colonic irrigations; in addition the patient had rest, a soft diet, etc. In two weeks he was put through another course of ipecac, receiving a little more this time. All through there were no amebas in the stools, the patient experienced very little pain. In another week he was given 80 grains more of salol-covered ipecac pills. That was last November. Seven months have elapsed and the patient has gained in weight and feels very different since his infection. To all intent and purposes he is absolutely well. In this case the interesting feature was the degree of ulceration in the lower bowel which could easily be seen with the sigmoidoscope. These ulcers are entirely healed. His stools are normal in gross appearance and in the course of repeated examinations I have never found a sign of an ameba. The other patient was a young soldier from the Philippines. He received a typical course of treatment, being given large doses of salol-covered ipecac pills. This patient was also irrigated because I felt that some benefit would result from flushing the large bowel. He, too, is well. I am sure that there are other cases like this in different parts of the country as far north as Michigan, but we fail not only to recognize these cases, but also to treat the patients by what I believe to be the only satisfactory method, namely, administration of large doses of ipecac.

DR. JAMES P. TUTTLE, New York: It is well to hear both sides of a subject such as this—the surgical as well as the medical. We who have had more experience in the local treatment of these conditions than those who have participated in the discussion thus far know that the results of local measures and of appendicostomy have been maligned here this afternoon; all our patients come to us for local measures and appendicostomies after failure to cure by medical measures alone. I have seen true amebic dysentery develop in people who had never been outside of a fifty-mile radius of New York City, and there is no longer any doubt that the disease

is frequent high up in the temperate zones. A patient was sent to me for diagnosis who had been treated by physicians in Philadelphia, Baltimore, Richmond and New York. All these men had amebic dysentery in view, but they had failed to discover the amebas. I took the patient and made a very careful local examination and could only find some small scars in the rectum, apparently such scars as are seen after dysentery. I sent this patient to the hospital and placed him in the laboratory. He was given large doses of salts and was told to stay there until his bowels moved. He remained there five hours and yet there occurred no movement of the bowel. The next day this was repeated and we got a stool in which was a mass said to be about the size of the thumb nail, which was alive with motile amebas. The stools must be examined in a fresh state and warm; also every stool should be strained in order to get the little mucus flakes in which the amebas are found. The patient, mentioned by Dr. Fletcher, who was operated on at Johns Hopkins Hospital, and in whom the appendicostomy failed to cure, turned up afterward in my office. I followed this patient carefully. In the appendix I found a rubber tube which had become almost vulcanized from being left in too long, and which stuck down five inches into the cecum. There were ulcers around the end of the tube where it was pressing. I also found in the lower end of the rectum a number of ulcers, not amebic at all, but the result of mixed infections, which did not require amebic treatment. They required simply local treatment for the subsequent infection which had followed the amebic infection. This was a traumatic ulcer and cure resulted from simple local treatment. I disavow any desire to perform an appendicostomy on an individual with amebic dysentery until there has been tried Epsom salts, ipecac, local washings with quinin solutions, etc. I do not think it makes much difference what solution is used so long as the temperature is below 70 F. I am using a different method. I do not advise operation until I have tried local treatment. But when I fail with the use of the local treatment and the patient comes back again in four or five months and shows that I have not reached the seat of the amebic infection, then I may propose operation. Washing out the colon through the appendix is effectual; it gives no mortality, while the reader of the paper confesses to a mortality of 17 per cent. under medical treatment. Over 125 of these patients have been treated in New York City, with but one death. This patient died from acute miliary tuberculosis after an appendicostomy. Not less than twenty officers of the United States Army, treated with ipecac and other medicines, were not cured; they then said, if these agents fail, let us try appendicostomy and see if we cannot be cured. The trouble with so many appendicostomy operations is that the operation is not done as it should be; an infection

occurs around the end of the appendix which, as a result, slips back into the abdomen. Another thing is that the opening is closed too quickly. In the United States Army men the openings are usually closed inside of three months. I never close them inside of six months, and in the majority of cases I leave them open permanently. The opening is a safety valve. It is easy to get a stool by running warm saline solution through the fistula. I only advise operation as a last resort. Recently I have had three patients with amebic dysentery. I treated them by administering a formalin solution, one dram to a quart of water; along with full doses of tannopin by mouth. After the administration of the medicines and washing out the bowel I have not been able to see any amebas after forty-eight hours' treatment in any one of these three cases. These patients have been under treatment four months, two months and one month respectively. So far there have been no recurrences. I am inclined to believe, however, that it would be well to use local irrigations and at the same time use ipecac.

Dr. Samuel G. Gant, New York: I wish to confirm Dr. Tuttle's statements regarding the usefulness of appendicostomy in the treatment of both the amebic and bacillary types of dysentery. This operation, however, would not be necessary except in rare instances in this class of cases if thorough colonic irrigations could be obtained otherwise. There is but a small number of medical practitioners, hospital internes and nurses who could effectively introduce the colon tube and wash out the bowel. Lack of training renders many unable to pass the tube beyond the obstructions offered by the sphincter muscle, rectal valves, and the angulation at the rectosigmoidal juncture. When the colon tube cannot be made to enter the upper part of the large intestine in the ordinary way, the sigmoidoscope should be introduced and the tube passed through it. Low irrigations diminish the number of stools but high washing of the bowel is imperative when a cure is anticipated. One must go even a step farther than this and place the patient in the Trendelenburg posture and then change him from one position to another to make the irrigation complete, because if this is not done the fluid will flow along one side of the gut and leave the lesions on the other untouched. In my opinion, the temperature of the solution has nothing to do with the healing quality of the irrigation and I prefer it at the bodily temperature because it is more comfortable; I have discontinued ice cold solutions because of the shock and great suffering which their employment frequently induces. I have successfully treated patients suffering from dysentery with solutions containing salt, quinin, ichthyol, kramaria, hydrastis, boric acid, permanganate of potash, formalin, silver nitrate and other medicaments in varying strengths, and I believe that the greatest benefit derived from any irrigating fluid is due to its mechanical effect

in cleansing the ulcers and removing toxins from the bowel. When the discharge is profuse and contains considerable pus and blood, in the beginning I prefer to wash the bowel out daily with a solution containing from 20 to 30 grains of silver nitrate to the quart, to be followed by flushing the bowel with a normal salt solution to lessen the tenesmus when necessary; when the movements have a very offensive odor, I correct this and encourage the ulcers to heal rapidly by employing a 2 per cent. solution of ichthyol. I hold that the dysenteric lesions in a few cases involve the lower ileum and that in others the dysentery has become grafted on an enterocolitis, and that under such circumstances it is imperative that the irigating fluid be made to reach the few lesions in the small bowel as well as the many ulcers in the colon. In such instances, and in cases in which, for any reason, the appendix is found unfitted for through and through irrigation, I recommend cecostomy, which provides a simple means of irrigating both the small and the large intestine, a procedure which has proved universally successful in my hands. So far as my experience goes, appendicostomy and cecostomy are far superior to diet, rest and all forms of medication, not only in dysentery, but in other types of colitis; and these surgical procedures should not be discarded in favor of the special treatment as many of the previous speakers would have us believe.

DR. SIDNEY K. SIMON, New Orleans: Our surgical friends have certainly added much of timely interest and value to the discussion of this important subject. At first it appeared we were going to have merely a love feast with ipecac as almost the sole article of diet. I believe that ipecac is best administered in one large dose, given in the evening, after a three-hours' fast. The plan of giving 5 grains, or 10 or 20 grains, three times a day, is not so good in my opinion as the one large dose. Formerly we also used opiates, but the employment of the salol-covered pill makes this in most instances unnecessary. I agree with Dr. Tuttle about finding the amebas in the warmed stools only. Neither do we find it necessary to strain the feces or to pick out the mucous flakes. On the contrary, all parts of the stool should be examined, as the mucous flakes do not always contain the largest number of amebas. I was not correctly understood regarding the mortality figures. Fifty cases were reported, mostly from hospital records, and not all my own, so that the treatment varied. In every patient not moribund treated by me with ipecac, the mortality has been nil. There is a certain tendency to recurrence in this as in all bowel infections. This should be explained to the patient with the understanding that perhaps a second course of treatment will be necessary. In one of my cases with a clear amebic history of eight years' standing,

there has been no recurrence for one year following the second ipecac treatment. After the patients have once been freed of amebas it is important to instruct them to boil the water they use to obviate the dangers of reinfection. After these patients are cured in the hospitals they might return to their former residence only to become reinfected with the original contaminated water supply. I trust that I have made clear the two points I wished especially to emphasize: the prevalence of the ameba over the entire country, and especially in the south, and the proved value of the ipecac treatment, rendering surgery in most instances unnecessary.

OPERATIVE TREATMENT FOR CIRRHOSIS OF THE LIVER

GEORGE DOCK, M.D.
NEW ORLEANS

Operative treatment for cirrhosis of the liver has engaged the interest of many physicians and surgeons since Talma proposed it twenty years ago. If it is not more frequently carried out, the reason may partly at least be found in the high mortality immediately following the operation or within the next two months. I shall not attempt a new statistical study, since this has been done well by several others within a recent period, but shall point out certain facts that need to be considered in connection with all novel operations and especially for those in diseases inevitably fatal, for alleviation of symptoms, and not with a view to radical cure.

The statistics of the Talma-Morison operation and its modifications and substitutes are unfavorable partly because many patients have been operated on too late to do good, and when the risk of failure was excessively great on account of other organic disease. Such a thing happens in all new operations, but, instead of stopping operative treatment altogether, it should, if the operation has a single thing in its favor, lead only to more careful selection, earlier diagnosis, and greater care in the operation and after-treatment. Moreover, the death-rate and the shortening of life must not be compared with similar incidents in persons previously healthy, or persons with trivial diseases. As in so many other border-line diseases, we should think chiefly of the pain

and disability, and the inevitable death within a time not very long, under the usual methods of treatment. From that standpoint, a single patient made comfortable for a time beyond the usual expectation outweighs many others whose days may have been lessened, though they lost nothing they ever could have gained in function. In such a case, it seems only fair to put the matter as plainly as possible before the patient, and to let him decide. Many, in the particular case now before us, will prefer the cathartic and the trocar, just as many others will refuse to stop the injurious habits against which they are warned. Some, however, will prefer a definite risk with the hope of relief, and it is in order to show what may be done even under many disadvantages that I bring the subject up at this time.

I have long been interested in the subject, but in most cases could not get the patient and surgeon to coincide. In some cases the one, in others the other, demurred. In one case I found what seemed an ideal subject, a man with recently developed ascites and distinct but not severe symptoms of cirrhosis, no cachexia, and no anomalies in the urine. Paracentesis gave a characteristic fluid and showed the liver not enlarged. After the situation was explained to the patient, he chose an operation, which was performed by an experienced surgeon with every appearance of technical accuracy. The liver was moderately cirrhotic, the spleen enlarged, the veins in the omentum and under the parietal peritoneum distended. Death occurred on the third day from septic peritonitis. Such an event is always discouraging, and it gives me all the greater pleasure to report another case in which the duration of life and maintenance of function seem unmistakably lengthened, notwithstanding many adverse circumstances. I cannot claim any credit for the result, which the patient owes to Dr. Edward Hamilton, of Houston, Texas. I simply have taken advantage of a clinical experiment, with the hope of encouraging others by the lesson it teaches.

REPORT OF CASE

Summary.—Symptoms of cirrhosis of the liver, with ascites following a history of hard work and hard drinking; patient tapped for ascites fourteen times, then had omentopexy, in December, 1902; was tapped ten times after that, up to June, 1903, and since that time has been able to do hard work, only at long intervals having symptoms, which are easily relieved by medicine.

History.—E. D. S., aged 49; single, railroad switchman, American, was admitted to the Charity Hospital, New Orleans, Jan. 7, 1909, on account of fulness of the abdomen, pain in the stomach, vomiting of a large quantity of blood, and tarry stools. The family history is unimportant. The patient had smallpox and gonorrhea at the age of 30, and during the next eighteen years several mild attacks of malarial fever. In 1892 he was shot while aiding the Cuban patriots, a rifle-ball going through the abdomen transversely just below the liver, but not near the portal vein, as indicated by the scars. There was constant oozing for twenty-four hours, but in a week the wounds healed and the patient had no further trouble from them. The patient has worked on railroads and in the oil fields, working hard most of the time, and exposed to risks from bad food and water, and malarious climates most of the time. He has chewed tobacco since the age of 10. He drank regularly but moderately up to fifteen years ago, when he began to get drunk about every four months, spending on drink all he had saved in the interval. The periods of intoxication averaged five to ten days, but were sometimes prolonged to two to four weeks. In 1902, while working in the Texas oil field, with poor food and great exposure, he began to feel bad, drowsy and tired, and developed a severe diarrhea which resisted treatment. In about three weeks the abdomen became swollen, and he then went to St. Joseph's Infirmary, Houston, Texas, for treatment. He was under the care of Dr. Edward Hamilton, to whom I am indebted for information regarding the operation, and also for the privilege of reporting the case. The diagnosis was cirrhosis of the liver. The ascites was severe, the abdomen measuring 45 inches when full, and tapping had to be done at short intervals—six to ten days. After he had been treated three months, and tapped fourteen times, the patient followed Dr. Hamilton's advice regarding an operation. "The abdomen was full of fluid, the arteries and veins of the omentum and peritoneum enormously distended, and the liver hard and nodular. The omentum was sutured with catgut on each side of the wound to the parietal peritoneum. The patient made a good recovery, but had to be

tapped ten times during the next four months, and left the hospital in June, 1903, six months after the operation." Six months later he appeared before Dr. Hamilton in order to undergo an examination as brakeman, " and would probably have passed if it had not been for the scars on his abdomen." (The quotations are from Dr. Hamilton's letter.) The abdomen then measured 32 inches. The patient worked in a malarial locality, had numerous attacks of fever, for which he took whisky, and from about five months after the operation he had again taken up the habit of frequent intoxication. In 1905 he had diarrhea, shortness of breath, distention of the abdomen and all his previous symptoms. After trying with no benefit the waters of various mineral springs, he came to the Charity Hospital, and left much improved after two months, having been treated with purgatives, principally jalap. He then remained perfectly well, working as switchman, until October, 1907. Then, having been drinking regularly, he had a return of symptoms, and a hemorrhage from the stomach, and returned to the Charity Hospital, under the care of Dr. John B. Elliott. There was moderate ascites, anemia, and slight icterus. The liver dullness was small; the organ could not be felt. Treatment with compound jalap powder again was followed by complete relief of symptoms, and the patient was able to do hard work again, carrying loads of 150 pounds. Later, a return of malaise and bad taste in the mouth led to drinking. This became worse in the fall of 1908, and a few days before the last admission the abdomen again grew large, there was pain after eating, and the stools were black but became natural before admission.

Examination.—On admission I found the patient almost free from subjective symptoms; temperature, pulse and respiration normal. There was slight emaciation, cachexia, skin was sallow, scleræ not yellow. The heart was in the normal position, the sounds weak but clear, the radial arteries tortuous. The lungs were negative; diaphragm shadow from the sixth to the seventh intercostal space on the right side; the seventh to the eighth on the left. The abdomen was slightly enlarged, one and a half inches above the level of the ribs. The superficial veins running up the middle of the abdomen, continuous with those on the thorax, were slightly enlarged. There was a scar in the median line, 7 cm. long, extending from 3 cm. above the umbilicus. This lay above an oval elevation, corresponding to a soft irregular mass beneath and adherent to the abdominal wall. The liver could be felt; the dulness was small. The spleen was slightly enlarged and hard. There was movable dulness in the abdomen, ris-

ing to the umbilicus on standing. There were no hemorrhoids. Urine and blood were negative.

Later Course of Disease.—Treatment was again carried out with compound jalap powder, by my colleague, Dr. J. B. Guthrie. There were no stomach symptoms and no blood in the stools. The distension subsided, though the superficial veins remained enlarged. After a short time the patient was able to assist in the ward work. He was then given a position in the pathological laboratory, later made night-doorman, and has remained well up to the present time.

I can not add anything to the theory of the effect of the operation. I am inclined to agree with Rolleston in attributing the benefit chiefly to the lessening of venous pressure, enabling the liver to deal more readily with the toxic substances passing through it, the improved arterial circulation following the reduction of venous pressure, and the greater chance of compensatory hyperplasia. So far as the ascites is concerned, it seems that in many cases the improvement of that may be due more to the effect of the operation on the serous membrane than to the opening of collateral paths for the blood.

From every point of view it is desirable to operate early, before the liver has undergone advanced degeneration, and before toxemia and disease of other organs have made the operation too dangerous. As to the details of the operation, I shall not discuss those that have been proposed by surgeons, but confine myself to the suggestion that in all cases the abdominal organs should be examined as carefully as possible, in order to furnish data of value in the analysis of future cases.

In view of H. Eichhorst's recent recommendation of cream of tartar[1] for cirrhosis, it is interesting to see how well the compound jalap powder seemed to do in the case now reported, taking down the ascites rather better, it seemed to me, than usual. Cream of tartar is an ingredient of compound powder of jalap, and has been much used alone as a laxative in such cases.

124 Baronne Street.

1. Eichhorst, H.: Med. Klin., 1909, No. 11.

ABSTRACT OF DISCUSSION

DR. NATHANIEL BOWDITCH POTTER, New York: I should like to speak of a patient operated on by Dr. George E. Brewer of New York at the City Hospital six years ago. The patient has been in my service at either the City or French Hospital nearly every year since the operation. This patient's life undoubtedly has been prolonged over five or six years.

DR. ALBERT E. ROUSSEL, Philadelphia: My experience with cases of this kind has not been so satisfactory as those that have been reported here. I have had under observation at different times probably eight or ten patients who have been operated on, and in those with distinct cirrhosis of the liver, with two exceptions, there has been no benefit. I think we should take into consideration the fact that occasionally the mere operation of tapping will result in establishing a compensatory circulation and enable the patient to live for a considerable period of time in fairly comfortable condition. I have such a case in mind now; in this case I made an unfavorable prognosis. After the first two tappings in which two gallons of fluid were removed, the patient, a woman, remained in good health for a period of five years. To be sure, these are exceptional cases, but they do occur, and consequently they should be borne in mind when the advisability of an operation is considered. Another very important point that should be borne in mind is that many of these patients have cirrhosis of the liver long before they come to us because of the ascites. In making examinations for life insurance, we know that there are a number of instances in which men, especially club men and individuals over 40 years old, have relatively large livers; very often such an enlarged liver is the early stage of atrophic cirrhosis or of fatty cirrhosis of the liver; but rarely is it, as often imagined, hypertrophic cirrhosis, which is a very rare disease. By careful dietary treatment in the early stages of the affection, by a removal of the cause, such as alcohol or over-eating, the process may be delayed for a very great period of time. It is unfortunate that no visible evidences of the disease can be demonstrated to the patient, such as albumin and casts, which appear in the urine, showing an interstitial nephritis. When this does occur in the last-named disease, however, the patients are really frightened, and they then may mend their ways. We know that people may have enlarged livers without having any definite symptoms pointing to the trouble. I think it is up to the man of the future to make a diagnosis of cirrhosis of the liver before the circulatory and toxic symptoms make their appearance; then medical and perhaps surgical treatment will give different and better results.

DR. CHARLES A. HOOVER, Cleveland: I should like to report one case. This patient was under observation thirteen years ago at the City Hospital in Cleveland. The man was tapped I believe about fifteen times at the hospital. The resident phy-

sician was in the habit of doing the paracentesis. When he completed his service at the hospital he went to practice in a neighboring town. This man with the ascites liked the manner in which the retiring physician had done the work, and so followed him to the town in which he started to practice. The doctor was in the habit of doing the operation once in about five days. One morning the patient with distended belly visited the physician in his office and requested a paracentesis. The doctor was busy at the time and said he would tap him that afternoon. But at noon the patient had a profuse hemorrhage from the bowels, losing great quantities of blood. Two hours after losing so much blood the man was very blanched; when the doctor arrived a friend of the patient was at the bedside, who said: "From my observation it seems strange to see him so bloodless, and yet he appears to have such a good pulse." The man died from anemia that same night. An autopsy was performed on the following day and the abdomen was found to be dry; every bit of the serum had been absorbed. Judging from the repeated tappings that had been done, not less than five liters of serum had been taken up. There was absolutely nothing here excepting the usual venous anastomoses and the lowered intravascular pressure to enter into the rapid absorption of fluid.

DR. SAMUEL E. MUNSON, Springfield, Ill.: Dr. Hoover's report of his case reminds me of a man, 60 years old, who had hepatic cirrhosis accompanied by tabes dorsalis, and who developed dropsy. For a period of almost one year I performed paracentesis about every seven or ten days. Sometimes I removed as much as six gallons of fluid. After a period of time following these tappings, the fluid disappeared and did not recur again. This man lived two or three years afterward. Death was due to tabes dorsalis.

DR. JOSEPH L. MILLER, Chicago: I have seen two cases of so-called cirrhosis of the liver cured after a few tappings. In one case it was found that the patient was suffering from tuberculous peritonitis. The second patient was supposed to be cured, but returned in a few months with a tuberculous peritonitis. It is my opinion that some of these cases of so-called cirrhosis of the liver reported cured by tapping are really cases of tuberculous peritonitis.

DR. GEORGE DOCK, New Orleans: It is very important to remember that ascites and cirrhosis of the liver do not mean the same thing; there may be cirrhosis of the liver without ascites. In any case we must not suppose that the ascites is the result of cirrhosis of the liver; this does not always follow. Many cases are diagnosed as cirrhosis of the liver and reported as cured by operation, or cured after repeated tappings, that are found afterward to be cases of tuberculous peritonitis or some other form of peritonitis. The advantage of an operation, however, is that it enables one to make an accurate

diagnosis. Dr. Hoover's report of this case is very interesting; but I would like to point out that often the ascites disappears without known cause and without treatment. I reported a case some years ago in which a patient was prepared for tapping to be done a few days later, and then there was nothing to tap for. The abdomen was flat and there were no signs of fluid in it. Two weeks later this patient died and no fluid was found in the abdomen. There was a secondary cancer of the peritoneum. With regard to whether the operation does any good in these cases, that is something I know no more about than anyone else. But the results of the operation, such as reported by Dr. Potter and others, and the results published in the literature, shown by improvement and sometimes recovery, we cannot get around. For a certain period of time there is no doubt that in some cases good results follow the operation. Dr. Rolleston's idea is that improvement in the circulation followed such an operation, thus enabling the patient to withstand the disease longer than he otherwise could. Talma discovered on the autopsy table that in those cases which pursued a favorable course in cirrhosis of the liver, new vessels had spontaneously formed which were capable of carrying on a collateral circulation. I have seen such a condition in a patient operated on a second time by Dr. Roswell Park. The vessels were enormously developed. I think that the major part of the benefit of the operation comes from changing the process in the peritoneum. Whether there is such a change as occurs in Bier's hyperemia treatment, I do not know; but the hyperemia may be an important part. In patients having a great deal of ascites and without much change in the liver, I should prefer having the operation done. My colleague, Dr. Matas, is now looking for a patient on whom he can make a direct anastomosis of the abdominal veins and send the blood around the liver. Such an operation as he proposes promises a great deal.

ALGID MALARIAL FEVER

WITH REPORT OF CASES

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The pernicious types of malaria are of absorbing interest because of their diverse clinical features and their high mortality. Complex problems are attractive, and a high death-rate in any disease is apt to stimulate the energies even of the slothful.

Pernicious malaria presents such problems, and their solution deserves the study of our best clinicians, for much more work is required to be done in their fuller elucidation. The term "pernicious malaria," while conveying an impression more or less definite, to the rank and file of the profession, and, therefore, to that extent serving a useful purpose, has none the less impressed me as being indefinite.

Perniciousness is a quality that may characterize any disease, and is doubtless dependent on a number of conditions. One might just as well speak of pernicious scarlet fever, pernicious measles, pernicious smallpox. Instead, however, we speak of malignant scarlatina, black measles, hemorrhagic smallpox.

CLASSIFICATION OF FORMS OF MALARIA

While these qualifying adjectives have in the main been inherited, and are not of the highest scientific value, they carry a sort of universal significance, which is, in a measure, understood. In this sense, therefore,

certain types of malaria have been described in all languages—at least in all countries in which they occur—as pernicious. I think that the tendency on the part of some clinicians to subdivide minutely this class is as confusing as unnecessary.

For instance, I think one might just as well speak of the diarrheal form of typhoid fever, or of the constipated form of pneumonia, as the diarrheal or dysenteric form of pernicious malaria, as contrasted with the algid form. The simpler the classification of any disease the more effective it is. There is a type of malaria that is always serious and in many instances fatal. To this, for want of a better name, the term pernicious has been given, and is everywhere generally accepted.

From my study of the classifications of others and from my own experience with this type of the disease, I think that a subdivision into the comatose, hemorrhagic and algid varieties is all that is needed either for accuracy or elasticity. I have seen no variety that could not be placed under one of these subdivisions. A multiplication of them is, therefore, not only unnecessary but confusing.

With the term "pernicious" more or less definitely understood, it is interesting to inquire into the causes of pernicious malaria. It is generally conceded that this type is produced by the action of the estivoautumnal variety of the *Plasmodium malariæ*. Why, then, are some of the cases produced by them mild or benignant and others severe or pernicious? Unfortunately, we must depend here on analogy and our knowledge of the life-history of the parasite.

First, we may assume that a great number of the invading parasites, with the toxins secreted by them, is sufficient to bring about the pernicious symptoms. Against this it may be argued that in many fatal cases few parasites have been found. In such cases it may be and probably is true that the parasites have collected in the internal organs.

Second, it may be argued that in the severe cases either the parasites possess an unusual virulence or the resisting power of the individual has been lessened by preceding attacks of this or some other disease, or some vice of constitution.

Third, it may be supposed that the parasites, for reasons unknown to us, tend to accumulate in some portions of the anatomy, interfering with the circulation there and causing greater absorption of their toxins, and that the character of the attack varies according to the point of chief attack.

This is not unknown in the case of other organisms and has been actually shown in this. I refer to what has been described as an apparently unusual stickiness of the organisms and sluggishness of the circulation in the part.

It may be that a part or all of these factors are operative. At any rate they furnish a not unreasonable working hypothesis for the varying clinical pictures as we encounter them. For instance, when the cerebral cortex is invaded through its circulation we have the comatose variety produced. When the basal ganglia and medulla are chiefly attacked we have the algid variety. When a more general (even though in cases less active) invasion occurs we have great corpuscular destruction, and hemorrhagic malaria or blackwater fever results.

All the pernicious forms of malaria are interesting, for they cry aloud for further study, but for the present our deliberations shall be limited to the algid type.

THE ALGID TYPE OF PERNICIOUS MALARIA

Algid malaria may be defined as a pernicious type of malaria, caused by the estivoautumnal form of the *Plasmodium malariæ* and characterized by profound prostration, cold and clammy skin, and an unclouded intellect; this latter in strong contrast with the comatose variety.

Geographic Distribution.—It occurs in all tropical and subtropical countries where malaria is found, occurring in Africa, Asia, southern Europe, the southern United States, Central America and South America. In predisposition, in age, sex and race, it does not differ from other forms of malaria. In subtropical countries it occurs chiefly in the late summer or early autumn and in all cases there is either the history or strong presumption that it has been preceded by other attacks of malaria; in other words, that it is a sequel or termination of a more or less chronic malaria, recognized or unrecognized. In all cases it is produced by the tertian and crescentic forms of the *Plasmodium malariæ.*

Pathology.—In cases in which autopsies have been performed, the pathology does not differ in any essential particular from that of other forms of pernicious malaria, with the single exception of hemorrhagic malaria, in which the urine is more or less surcharged with hemoglobin, giving to it its red and darkened color, and also its name, blackwater fever.

Symptomatology.—The symptoms of algid malaria are clear-cut and definite, and from them it gets its name. In some cases a definite malarial history will be elicited; in others the patient may not have been conscious of other malarial paroxysms, but he lives in a malarial section or has recently come from one.

The attack may be preceded by feelings of malaise, loss of strength, weight and appetite. A more or less torpid liver and constipation are also precursors, though more usually choleraic symptoms usher in the attack. The attack is often preceded by a more or less torpid liver and constipation. The immediate attack is ushered in by a chill or a general sense of chilliness and discomfort, in which event the chill is usually neither so decisive nor so long as in the intermittent variety. Following this there is a rise of temperature, which is usually not great; in most cases it is not present, and cases have

been recorded in which the temperature remained subnormal.

The tongue is usually dry and coated and thirst is great. With the onset of the paroxysm pronounced nausea, vomiting and diarrhea set in. The general prostration is profound, and, while headache, pains in the back and limbs are usually present, they are not so marked as in many of the more benign varieties.

The facies is that of a patient suffering from cholera. The face wears a pinched look; the eyes are abnormally bright with hollows and circles around them; and, singularly enough, the brain remains abnormally bright even unto the end. The conjunctivæ and skin are often yellow. The skin is cold and clammy and shrivelled and almost constantly bathed in sweat, so that, to the touch, the patient feels as if he did not have any fever. It is this phase of the condition which gives to the disease its name. The mouth and rectal temperature may, however, show an elevation of temperature varying from 99 to 103 F. The pulse is small and thready and toward the end may be imperceptible. There is usually loss of appetite, and great thirst exists. The urine is usually scanty, high-colored and may show albumin and casts, but does not contain hemoglobin. The diagnosis is made from the history, which naturally includes the patient's past history, the presence or absence of cholera in the region and cholera morbus or ptomain poisoning. After all has been said, the diagnosis will necessarily hang on the blood examination or the autopsy; and even these may be misleading, for a patient may develop ptomain poisoning and still have been already infected with severe malarial poisoning. Cases for reasonable doubt, however, are exceptional.

Prognosis.—The prognosis is generally grave. In my experience the mortality has been, I regret to say, 100 per cent.

Treatment.—In all forms of pernicious malaria quinin seems singularly ineffective. I still adhere to the ad-

ministration of quinin in the type under consideration, believing that it is a matter of the amount given and its subsequent absorption. For this reason I administer it hypodermically. The rest of the treatment is supporting and symptomatic.

REPORT OF CASES

CASE 1.—*History.*—H. D. V., white, aged 57, American, book agent, entered the City Hospital Oct. 13, 1902. His mother died of bilious fever, and one of his children died of malarial fever; otherwise the family history and personal medical history were negative. For about nine days previous to the patient's entrance into the hospital, he had been suffering from more or less nausea, vomiting, and swimming in the head, muscular weakness, and loss of appetite, which he attributed to the eating of some ham, which disagreed with him; following the nausea and vomiting, he developed diarrhea.

Examination.—On admission the patient was found to be a man of medium build, imperfectly nourished and anemic. The pallor of his skin was quite marked, the tongue coated and the conjunctivæ slightly tinged yellow. The lungs were normal, as was also the heart, except for diminished muscular power. The liver was slightly enlarged and the spleen considerably so. The skin was cool and clammy to the touch, being bathed in more or less profuse sweat; so that to feel the patient in any portion of his body, whether head, hands or feet, he seemed to be free from fever, and this continued steadily until the end. The temperature by mouth was 97.06 F.

Course of Disease.—On the next day the temperature rose to 98; then came a sudden drop to 93.06 at which time the patient developed a hiccough which persisted practically without intermission until his death. Nausea and diarrhea were pronounced. Following the drop in temperature there was a rise to 102.04 (by the rectum) although when the internal temperature was this high the surface was blanched, moist to the touch, and cool. Following this rise the temperature dropped to normal, and continued so until the morning of the fourth day. Just before death, the rectal temperature registered 100. The patient's mind continued unnaturally bright until the end. The case presented a picture not unlike that of Asiatic cholera, except for the fact that the stools were not so numerous or profuse. The diagnosis of algid malaria was made from the blood-smear,

in which great numbers of estivoautumnal tertian organisms with crescents were found. Treatment was unavailing; at the beginning he was given broken doses of calomel at fifteen minutes' interval until he had received a grain and a half; he was given, hypodermically, ten grains of acid quinin hydrochlorid with urea three times a day, and a supporting treatment, including high salt enemas. Unfortunately, an autopsy was not allowed by the family.

I find a case recorded[1] by Dr. R. H. von Esdorf which presents many points of resemblance to the case just recorded by me, except for the more pronounced choleraic discharges in Dr. von Esdorf's case. Fortunately in that case an autopsy was thoroughly performed and recorded.

CASE 2 (von Esdorf's).—In brief there was a history of an illness of about six hours; symptoms of cholera, no fever, syncope and death.

Autopsy.—Enlarged liver and spleen; discolored mucous membrane of stomach; discolored mesentery and omentum, section of liver and spleen showed hemozoin in large and small masses, young small ring form of malarial parasites in red blood cells, lymphocytosis; free hemozoin in blood.

In a letter Dr. Rosenau makes this pertinent remark to Dr. von Esdorf, and the deduction seems reasonable: "He surely had an access of pernicious [malaria]. Don't you suppose, however, that he might have been sick on the trip, and that when you saw him he was suffering with the stupor due to the clogging of the capillaries of the brain with malarial pigment and parasites?"

CASE 3.—*History.*—Mr. B., aged 60, white, travelling salesman, admitted to City Hospital, Oct. 16, 1902. His previous history was negative. On admission patient had severe bilious vomiting, copious diarrhea, and pains in stomach and intestines.

Examination.—The patient's temperature was 95 F. on admission and remained subnormal until death. The pulse was small and thready; respiration 28 to 40. The skin was cold, moist, clammy. The intellect was clear.

1. Von Esdorf: Boston. Med. and Surg. Jour., June 18, 1908, clviii, 937.

Course of Disease.—The patient was given acid quinin hydrochlorid hypodermically, Fowler's solution and a supporting treatment, but died on the third day. An autopsy could not be obtained.

For the report of the following case I am indebted to my friend, Dr. Murphy:

CASE 4.—*History.*—John W., colored, aged 19, laborer in brickyard, was admitted to Lamar Hospital Sept. 26, 1902, in profound collapse.

Examination.—The patient was with a history of having had one chill eight days before admission, when diarrhea and nausea set in after a chill; conscious; his skin was cold and clammy; there was nausea, vomiting of green material, and copious watery diarrhea. The spleen was enlarged; the abdomen retracted; there was marked pallor of mucous membrane. Pulse was 124 to 126; temperature 97.8. Blood examination showed profuse infection with estivoautumnal ring forms, also a few crescentic and ovoid forms.

Course of Disease.—The patient was treated with calomel and magnesium sulphate after washing out stomach, and given acid quinin hydrochlorid gr. xv. hypodermically every three hours for three doses. Remittent fever set in after patient rallied from collapse, but yielded to treatment without any return of algid symptoms after twelve days.

CASE 5.—*History.*—Susan Jones, colored, aged 56, laundress, was admitted to Lamar Hospital, August 1900, with history from family of "dysentery," with nausea and vomiting for three days. Coma had set in three hours before admission to hospital.

Examination.—The patient was unconscious on admission. Temperature was 98; pulse 108; respirations 20. Blood examination showed numerous pigmented leucocytes, but no intracellular parasites.

Patient sank into deeper and deeper coma and died nine hours after admission to hospital.

Autopsy.—This showed enlargement of liver two fingers' breadth below costal border, spleen just below costal border, dark red in color; capsule tense, soft in consistency; no changes of importance in other organs; liver and kidneys showed cloudy swelling. Smears from spleen showed enormous quantities of estivoautumnal parasites and pigmented cells, also much free malarial pigment.

503 Greene street.

ABSTRACT OF DISCUSSION

DR. JOHN A. WITHERSPOON, Nashville, Tenn.: While I do not practice in a malarial section of the country, I see much pernicious malaria in Nashville. The cases described by Dr. Coleman are comparatively rare and seemed to be those that are overwhelmed by the toxemia of malaria. Algid malaria, strictly speaking, is the type of malaria he described; in this type of the disease we find choleraic diarrhea, nausea, vomiting, colic, rice-water vomiting, purging and cholera. Fortunately, these cases are rare. In all malarial countries there are latent malarial cases; the infection invades the blood, especially of the spleen; the peripheral circulation may be examined carefully and no plasmodium found. Yet there is a low grade of infection and occasionally the temperature and chill will repeat themselves. Any man who undertakes to handle latent malaria should remember that it requires four or five months' constant treatment, and even then he may have relapses. One of the greatest mistakes a person may make in the treatment of this disease is to give quinin for two or three weeks and expect to cure the patient. Again, it should be borne in mind that these walking cases of latent malaria cannot be properly cared for while the patient is up and about his business. I have seen but two cases of the type described by Dr. Coleman. The first patient died one hour after I reached the bedside; the other lived thirty-six hours. Both patients were overwhelmed by the toxemia of malaria. The pupils were dilated, the rectal temperature was subnormal, the diarrhea was profuse and emaciation was rapid; yet the intelligence was perfect until the last. It is strange that with such a degree of prostration, with the pulse almost imperceptible at the wrist, the intelligence remained good. These patients rapidly became cyanotic and died in a state of extreme toxemia and exhaustion. It seems to me that the only hope for treatment in the type described by Dr. Coleman is to recognize the fact that the person has come to a malarial portion of the country, has come to an infected district where such severe forms of malaria develop, and that the only hope lies in trying to prevent the disease occurring. After the disease has developed, I believe that the only hope lies in the use of saline irrigations, transfusions and injections. I believe that the deep hypodermic injection of quinin, which gives such beautiful results in other forms of malaria, is absolutely useless here. Our only hope in curing these patients, I believe, rests in the intravenous injections of solutions of quinin. If the solution of quinin is injected into the tissues, into the muscular structures, the quinin will not be taken up by the circulation.

For those who are not used to giving quinin I should like to mention one practical point. I believe that quinin is used in too large doses. From 15 to 20 grains is sufficient in most

cases, although I have given as much as 140 grains in three hours. But I insist on giving quinin hypodermically, putting it deep into the tissues. I cannot hope to get such good results by simply putting it under the skin. There will not be any abscess or irritation of the skin and the quinin will be better absorbed. Those men who have condemned the hypodermic method in the treatment of these cases did not use quinin in a proper acid solution and did not insert the needle deeply enough in the tissues. If I get another case of algid malaria I shall introduce the quinin into the veins. Some patients recover because of their strong resisting power, so it is said; but I think if they do recover it is by the grace of God.

Malaria throughout the South is decreasing; the number of cases occurring is growing less and less. Clearing up the swamps in certain districts has lessened materially the number of cases of pernicious malaria. The disease is now practically limited to the swampy districts; it is here that blood becomes contaminated after the individual has been put to sleep by the melodious song of the mosquito.

DR. JAMES B. MCELROY, Memphis, Tenn.: I should like to speak about the classification of pernicious malaria and the treatment of the special form under discussion. The best classification probably is that given by Dr. Coleman, that is, comatose, algid and hemorrhagic. I think, however, that "blackwater fever" should be excluded from the latter. Blackwater fever differs from pernicious malaria in the mode of occurrence, in clinical manifestations and in parasitology. "Blackwater fever" occurs most frequently in old residents in malarial districts; pernicious malaria most frequently in children and newcomers to infected districts. In pernicious malaria, paroxysms occur at regular intervals of rarely less than twenty-four hours, and each paroxysm tends toward death. In hemoglobinuric fever the paroxysms usually come at shorter intervals, and, unless the first paroxysm ends fatally, death is not usually produced by the associated malaria. As a rule, pernicious attacks of malaria are associated with numerous parasites, with a tendency to increase with each succeeding paroxysm. Large phagocytes are also frequently seen. In blackwater fever parasites are few, and frequently absent; they tend to disappear early from the peripheral blood and internal organs as well; large phagocytes are seldom seen. While blackwater fever is most frequently of malarial origin, I do not think it should be regarded as a pernicious attack in the sense in which the comatose, algid and hemorrhagic are. The pernicious hemorrhagic group should be reserved for those pernicious attacks of malaria associated with real hemorrhages. The treatment best adapted for the algid forms is the prompt administration of quinin by hypodermoclysis in normal salt solution. The prog-

nosis is always grave in these; but on several occasions I have seen recovery follow this measure in severe algid attacks.

DR. THOMAS D. COLEMAN, Augusta, Ga.: I should like to call attention to the fact that in the cases I have reported the duration of the disease was short. In one case the patient died within a few hours after the onset. No case lasted more than four days. The duration was short and, of course, the symptoms were correspondingly severe and pronounced.

I prefer the bimuriate of quinin with urea, from 10 to 15 grains to the dose, repeated as the symptoms require. I think that Dr. McElroy's point on blackwater fever is a good one. I have never approved of the term "blackwater fever."

THE DIAGNOSTIC IMPORTANCE OF EXAMINATION OF THE FECES

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INTRODUCTION

At the present time when the medical laboratory men are following Ehrlich and Wright into the fourth dimension of medical science, when clinicians cry for a "dead-sure" test and when all demand nice, "new," clean work, it would seem a thankless task to spend fifteen minutes in talking about stool examination. I also would much prefer as subject the "complement fixation of this," "or the opsonic index of that," etc.; but a varied experience in clinical laboratories has taught me the importance of stool examination, and its growing importance now that functional diagnosis is rightly demanding more and more attention. While I was in charge of a clinical laboratory to which specimens were sent from all directions, many mistakes by physicians came to my notice, of which the following are a few illustrations: a strip of mucus was mistaken for a "decomposed tapeworm"; normal meconium was called blood; a roundworm six inches long was diagnosed as hookworm because it resembled a much-enlarged picture of uncinaria; solid fat was not recognized at all; soap globules and vegetable cells were called eggs, and eggs of harmless saprophytes were considered those of pathogenic parasites. But stool examination is fast assuming a new and very practical importance. Functional diagnosis is the subject of the future. We now no longer

ask merely, "What is the matter?" but also, "How much is it the matter?" and to gain any idea of the functional ability of the stomach, bowel, pancreas and liver, the stools must be studied.

My paper is not so much for the general practitioner who is willing to remain ignorant of the difference between an antigen-amboceptor combination and a thermostable immune opsonin, but who does know mucus when he sees it, as it is for those younger than I who lose the valuable information which stool examination might give them.

In the following paper I shall speak only of those findings which are of value to the busy general practitioner, omitting those methods of investigation which are reserved for the clinical laboratory.

At the onset permit me to emphasize one test which is very important; in fact, is the basis of all stool-work; the determination of the number of hours required for food to pass from mouth to rectum. This is easily determined by giving the patient with breakfast about one dram of charcoal or a little carmine. These are easily recognized in the stool. In some groups of cases it is well to use this test as a routine, and the results are often interesting.

This test may be used to test the presence of the so-called "latent constipation." In this condition it is supposed that while there is a normal-appearing stool every day and, therefore, no suspicion of constipation, yet the intestine contains always the feces of two or three days instead of but one, and each stool is, therefore, the refuse of the third or fourth day before instead of the second. While I would not try to be positive I do not believe in this idea.

MACROSCOPIC EXAMINATION OF STOOLS

It is from the inspection of a stool that one gets the most information. How few physicians ever look at the stools of their patients! How many are content with

the nurse's stereotyped description, e. g., "a moderately large, fairly well-formed stool."

In certain conditions the appearance alone of some (but not all) of the stools of some (but not all) patients suffering from these diseases is at certain stages (but not all) of these diseases sufficient for diagnosis. But because the appearance of all the stools is not diagnostic one should not refuse the aid occasionally given.

As a rule the patient needs no aid in making this diagnosis of constipation, but it is otherwise with those who think their periods of constipation normal and who complain of the brief periods of diarrhea. These persons illustrate the old and very true, if not strictly medical, French adage that "diarrhea is one of the best symptoms of constipation." The stools in this condition are rather characteristic, since in the fluid stool are seen flecks of mucus and small, hard fecal masses which are evidently broken off from impacted masses higher up which cause irritation and so the diarrhea.

In mucous colitis, mucus is passed with the stools, sometimes a few shreds, sometimes many and in some cases the stool consists of nothing but mucus. One patient recently passed nearly a pint of mucus in one stool. Some think that they have passed pieces of bowel. These strings of mucus should be searched for in all doubtful cases with abdominal pain. Unfortunately general practitioners too often fail to look for them, or do not appreciate their significance. The nature and the differences between mucous colitis and membranous enteritis, if differences there be, can not be discussed here, but even the most conservative will admit that the nervous element in both is of great importance, while the most radical will maintain that, except in a few cases due to pelvic tumor, mucous colitis is always a purely functional neurosis. Over 95 per cent. of the patients are nervous women and should be treated as such and the local bowel condition left alone. Were their stools examined for mucus, very many of these

women would escape operations for appendicitis, renal colic, floating kidney, gallstones, and ovarian troubles, one or each in succession, since the colic of mucous colitis can simulate each of these troubles. During the past year there have come under my personal observation roughly two thousand nervous women, and the history some give is very sad. They have had from one to ten operations performed on their abdominal and pelvic organs, and yet give clear histories of mucous colitis antedating their first operation. I feel this so strongly that in all doubtful cases suggesting any one of the above conditions I question carefully for the history of mucous stools, and in case these are or have been present will consent to operation only when the indications of a local trouble demanding operation are very conclusive.

The rare and interesting condition of intestinal sand does not attract nearly as much attention as it deserves. Intestinal sand is the name given to the sediment of fine granules which sometimes settle in a fresh liquid stool. These granules are from 1 to 2 mm. in diameter, are dark red, green or black in color, are spherical or slightly irregular in outline, and very hard. They are often present in great abundance, even half an ounce in one stool. Examined chemically, they have been found to consist of the phosphates and carbonates of calcium especially, but also of magnesium, iron, etc. A little organic matter, fat, cholesterin, and also bacteria are present in them. In one case they consisted of calcium sulphate. Those I have examined chemically consisted of a little plug of epithelial cells impregnated with carbonate salts. When but a few granules are present there is often a question as to the correctness of the diagnosis. Pseudosand is common. This may be the seeds of small fruits, various food adulterations, and various vegetable structures. The lower power of the microscope would easily detect the difference, and yet raspberry and similar seeds (perhaps timothy-grass seeds) have been sent to use for diagnosis. Intestinal sand appears intermit-

tently in the liquid stools of some nervous persons. It may or may not be associated with mucus. It is perhaps due to a secretory neurosis and has the same significance as mucus.

A definite colitis is usually indicated by the presence in the stools of pus- and blood-containing mucus. Whether or not there is increased frequency of evacuation will depend on the portion of the colon involved. Rosenheim has recently emphasized the relation between the portion of bowel involved and the symptoms. There is a form of colitis of the descending colon and sigmoid flexure especially, in which the stools are almost characteristic. Food is evacuated in from five to eight hours after ingestion. Its color, the test for bilirubin and the appearance of the muscle fibers and vegetable tissues on microscopic examination show that digestion in the small bowel is practically normal. The stools are soupy in consistency and contain many small masses of blood-stained mucus. On microscopic examination the red cells and leucocytes in the mucus cells are found to be in almost perfect condition. The stools are not very frequent, perhaps four or five a day, which is evidence of a normal rectum. This condition in one case now under observation has continued for over twenty years, without any periods of constipation, which differentiate it from the amebic colitis, and with little influence on the general health.[1]

In cases of rectal carcinoma the stools are very frequent and contain much blood and some mucus.

In all cases the feces of mucus should be studied for amebæ.

In the case of children the stools of blood-stained mucus should always suggest the possibility of intussusception.

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1. At autopsy the colon from just above the cecum to the sigmoid was uniformly small, scarcely admitting the finger. Its mucosa seemed in the main replaced by scar tissue in which were innumerable small bleeding points. The patient died of carcinoma of the cecum. There was no evidence of tuberculosis or amebic dysentery.

Acholic stools are usually betrayed by their clay color, soft consistency and foul odor. They mean obstruction of the common duct. But somewhat similar-appearing stools are passed by persons on a milk diet, or other diet rich in fat. The stools in a case of violent diarrhea may be colorless. In some cases the putty-like stools are due to bacterial fermentation which have changed the bile pigments to leucourobilin. In the latter case the color will return if the stool stand in the open air. Bile in abundance can often be extracted by alcohol and ether from a stool the appearance of which would suggest its absence. When a common duct obstruction is suddenly relieved the stool sometimes has a bright orange color, due to bilirubin which normally is never present in any amount.

Fatty stools may indicate several possibilities. Large amounts of fat are present in acholic stools and in those of a person on a milk diet or a diet including much cod-liver-oil or olive-oil. The fatty stools of patients with diseases of the intestinal wall which prevent absorption, as tuberculosis or malignant diseases of the retroperitoneal lymph glands which blocks the flow of lymph are often of great aid in diagnosis. But true steatorrhea is present practically only in cases with total destruction of the pancreas and not always then. The fat of these stools resembles melted butter and hardens at once on cooling. The stools most characteristic of pancreatic disease are those described by Ury and Alexander. These are fairly solid and contain a great deal of visible fat, much muscle fiber, and are the stools of patients who are not jaundiced. But the large bulky, fetid, greasy stools, the volume of which seems out of all proportion to the amount of food eaten, which show signs of active fermentation and which contain gross masses of undigested meat and vegetables, are also very characteristic of deficient pancreatic fluid, and should be looked for in cases of malnutrition.

In pancreatic disease the inspection of the stools often gives very important information. In acute hemorrhagic pancreatitis an intractable constipation usually obtains at first; then, if the patient lives, a diarrhea which is just as intractable. The stools may or may not be acholic. In five cases from literature fat was grossly visible. In gangrenous pancreatitis a persistent diarrhea, sometimes with involuntary stools, is the rule. The movements are thin, copious, very fetid and in one case green, much resembling vomitus. In three cases abundant blood was present.

In abscess of the pancreas the diarrhea is very severe. The movements are profuse, watery, fetid, although in some cases they are solid and very offensive. In one fatal case there were over twenty movements a day. In one case there occurred a profuse hemorrhage, about 1,000 c.c., from the bowel. In only one case was fat recorded, while in several cases pus was grossly visible. In cases of pancreatic cyst the stools will depend on the injury the pancreas has suffered. The stools are usually normal, but in five a definite steatorrhea was present. The diarrhea pancreatica which accompanies the evacuation of the cyst through the bowel is especially interesting. Late in a case of chronic pancreatitis, diarrhea is the rule. The stools are pale in color, of offensive odor, contain much undigested food and sometimes rather large lumps of fat. Blood is sometimes present in the stools. In cancer of the pancreas the stools may be normal, but steatorrhea and azotorrhea often are present near the end. In 13 cases of calculus of the pancreas with subsequent atrophy, blood was present in the stools of 4, and fat in those of 3.

The tarry stools in cases of gastric and duodenal ulcer are characteristic of severe hemorrhage in the upper alimentary tract. One practically never sees really tarry stools in typhoid fever; in the most of these cases the blood is fairly bright. But the stools may be fairly black when the patient is taking bismuth subnitrate or

after they have stood for a time in the air, if he is taking iron.

Gall-stones should always be searched for in the stools of a case of suspected gall-stone colic. The stool should be mixed with water and strained through a coarse mesh. Failure to find the stone may mean that the right stool was not examined, that the stone was soft and disintegrated in the bowel, or—and this is most important—that the colic is due to some other cause. In this connection should be mentioned pseudogall-stones. Of these the fat concretions are most important. These may be from a pea to a hazelnut in size and consist of fat of high melting-point. They may follow a meal rich in pork fat, mutton-fat, tallow, etc., but the most are seen in the stools of a person taking much olive-oil. It is these pseudostones which give this oil its undeserved reputation as of value in helping the gall-stone to pass. Also masses of vegetable and especially of fruit tissue may appear as concretions and they are sometimes harder than gall-stones. It is well to split open a suspected gall-stone and to examine its fractured surface, or to dissolve a little of it in boiling alcohol and to obtain cholesterin crystals when the alcohol cools.

The curds seen in the stools of infants and of adults on the milk diet are usually said to consist of casein and are interpreted as evidence that milk is not well borne. But these "casein-curds" often consist of almost pure fat.

One never in a normal stool finds gross particles of meat, bread or potato. These may be present in diarrhea due to any cause, but if they are seen in a firm stool the evidence is in favor of pancreatic disease.

The normal stool may contain visible masses of soaps—the yellow masses of calcium soaps, and masses of colorless soaps.

The study of intestinal worms is of growing importance. The ordinary roundworm and links of the tapeworm are readily recognized. It is well to remember that

decomposing tapeworm-links are practically never found in a fresh stool. That which suggests this diagnosis is almost invariably a string of mucus. To find the head of the worm it is best to shake up the stool in water and allow it to settle. All fragments of the worm will promptly sink to the bottom.

Tænia solium is in this country an exceedingly rare worm. I know of but one certain case. But one is often tempted to make this diagnosis, since the over-ripe segments of the *Tænia saginata* would appear to have a uterus with few coarse branches. An expert recently visiting the museums of some of our medical schools was able to find no specimen of *Tænia solium*. Of thirteen specimens thus labeled, eleven labels were certainly incorrect and the other two worms were too decomposed for identification.

To find the smaller worms, the stool should be well spread on a porcelain plate. Oxyuris, contrary to popular belief, does inhabit the intestine as high as the cecum or even higher, and may be found in the body of the stool. *Uncinaria americana* and *duodenalis* can easily be differentiated under a dissecting microscope if one take trouble to examine the head and caudal bursa. The reason why adult trichinas and whipworms have not been found oftener is that they have seldom been looked for.

THE MICROSCOPIC EXAMINATION OF THE STOOL

This is really the only method which the clinician can use to judge of the functional ability of the digestive organs, since accurate metabolism work is impossible for him. But to form a correct estimate the patient must be on a special test diet. That to be recommended is the Strasburger and Schmidt diet. To examine the stool microscopically the particles to be examined should be selected with care. If the stools are mixed with water and spread on a plate the choice often is easily made. If not, the stool may be mixed with water in a glass jar. The mucus will tend to rise to the

surface together with some of the vegetable tissue. Parasites' eggs will sink together with fragments of food, meat especially. From this water suspension may easily be selected particles for further study. The variety of objects which may be found on microscopic examination of the stool is unlimited. It will depend on the food eaten, on extraneous matter eaten with the food, on substances contributed by the digestive organs, on the flora and fauna of the alimentary canal, and lastly on the extraneous matter which adds itself to the stool after it is evacuated. This means that the microscopist may run across almost anything. He should be able to recognize vegetable tissue in general, especially the common forms of fiber. Especially should he be able to recognize chlorophyl-containing cells. The spiral cells are easy to recognize; the guard cells of leaves have been taken for fragments of carcinoma. The thorns of the down on some fruits are often diagnosed as worm embryos, while single cells, spores, pollen, etc., are often mistaken for eggs. Unfertilized eggs often do look very much like vegetable cells. Muscle fibers with the cross-striation well preserved are easy to recognize, but those partially digested are more difficult. It is important to be able to judge roughly whether an unusual number of fibers have appeared in the stool and if they show signs of insufficient digestion, for the condition known as azotorrhea is important in the diagnosis of pancreatic disease. By this we mean the presence in a firm stool of an unusual amount of undigested muscle.

One who systematically examines stools will surely find many eggs and larvæ which he can not recognize. The great wonder is he does not find these oftener. Two easy mistakes are thinking that the eggs of *Tyroglyphus siro,* or the flour mite, are those of *Bothriocephalus latus* and mistaking the larvæ of many dipteræ for the rather serious screw-worm. The number of dipteræ and other insects which have access to food and to the raw materials of which food is made is great. Here they lay

their eggs or add their bodies to the dish. In the stool one finds eggs, larvæ, perfect insects, and fragments of these. But the insect contaminations of greatest importance are those which are added to the fresh stool if it is not carefully covered as soon as evacuated. Fortunately we can usually recognize these as accidental findings. If in doubt one can always refer the specimen to the experts at Washington. In general these extraneous saprophytes' eggs are larger than those of pathogenic parasites. But just as serious is the danger of interpreting vegetable cells and even some soap masses for eggs.

The work of careful men has shown what a large number of persons are the hosts of animal parasites. *Ascaris lumbricoides* was found in about 0.4 per cent. of all examined, *Oxyuris vermicularis* in 0.8 per cent., strongyloid worms in 0.6 per cent., *Trichocephalus trichiurus* in 10.3 per cent., and *Uncinaria* in even 3 per cent. of all examined in some portions of the South. The eggs of *Ascaris lumbricoides* occur in large numbers in the stools of infected persons. When fertilized they are very characteristic, but the unfertilized eggs are often mistaken for vegetable cells. The eggs of *Oxyuris vermicularis* may be found in the stools, but more often in shreds of mucus on the surface of the stool and still more often in the scrapings from the margins of the anus. The eggs of *Uncinaria duodenalis* and *Uncinaria americana* are exceedingly important, since the anemia these worms produce is now recognized as a disease of national importance.

In searching for eggs the temptation is to pick out for examination a fragment of feces at random. But when in doubt the stool should be mixed with water, sedimented or centrifugalized and the sediment examined. It is often wise to give a dose of santonin or thymol to aid in the search for worms. If an infection with *Strongyloides intestinalis* is suspected the stool should be placed in a dish, a small depression made on

its surface, this filled with water and the stool left in a thermostat over night. If embryos are present they are easily found as eel-like worms actively swimming in this water. The eggs of these worms are seldom found in the stools. Of the protozoan parasites the various flagellata and ciliata are usually easy to find because of the commotion they make. *Amœba coli* is an exception to this. The stools, or better still the mucus which the eye of a rectal tube scrapes from the rectal wall should be examined while very fresh and, during the winter, before it has chilled. One examines the flecks of blood-stained mucus, if such there are; if not, the liquid portions of the stool. Definite ameboid motion, by which we mean the extension of a hyalin pseudopod from a granular endosarc, should be demanded. If in doubt the safest rule is always to discard the doubtful cell. One learns much now of the nonpathogenic *Entamœba coli* and the pathogenic *Entamœba dysenteriæ,* and of the encysted stages of the latter; but for the clinician these terms are only interesting reading. If he finds a small ameba, without hyalin ectosarc, in the fluid part of the stool, not associated with blood and mucus, and in a case the symptoms of which are not those suggesting amebic dysentery, he may possibly be safe in calling it the harmless *Entamœba coli.* Fortunately, however, during acute exacerbations the amebas are often numerous, are found in flecks of blood-stained mucus and themselves often contain one or more red blood cells. Clinically cases of amebic dysentery are characterized by chronicity and the tendency to relapse. The cases of great importance are those of amebic abscess of the liver and yet in patients who give no history of dysentery. The stools of all cases of suspected liver abscess should be carefully examined.

Pus in the stools is seldom recognized grossly, but the mucus flakes clouded with pus cells are helpful in the diagnosis of ulcers low in the small bowel and colon.

Red blood cells are usually seen in the mucus. From the condition of these red cells and the conditions of the leucocytes one can easily get an idea as to the source of the mucus. Charcot-Leyden crystals, if numerous, are important as suggesting an animal parasite.

Those who cling to the possibility of an autointoxication from the intestine are still making cultures of the stools for bacteria. As is well known, bacteria may make up even one-third of the dried stool. Many of these are dead and most cannot be demonstrated as alive by any of the common methods of investigation. These bacteria of the bowel contents may be classified as the normal flora, the harmless organisms accidentally swallowed with food, and those causing disease. Among the flora are *Bacillus lactis aerogenes* from the upper bowel, and *Bacillus coli communis* from the lower, *Bacillus subtilis, Bacillus alkaligenes,* and, for the suckling, *Bacillus bifidus.* Various thermophilic and acidophilic organisms may occur in great numbers.

Among the interesting pathogenic organisms which are frequently found are *Bacillus pyocyaneus,* the various staphylococci, streptococci, *Bacillus tetani, Bacillus aerogenes capsulatus* and *Bacillus tuberculosis.* That many of these pathogenic organisms, especially the streptococci and staphylococci, are almost normal flora, is seen by their almost constant presence in appendix abscesses and in the peritoneal pus in cases of perforation of the bowel. *Bacillus tetani, Bacillus aerogenes capsulatus, Bacillus bifidus* and *Bacillus subtilis* are some of the important Gram-positive organisms which have attracted attention recently in cases of pernicious anemia. In cases of suspected tuberculous enteritis it is important to search for the tubercle bacillus. To fail to find it has but little value. In cases of pulmonary tuberculosis, bacilli may often be found in the stools. To search for this bacillus it is well to examine any particles of mucus which may be present, but to digest a stool is seldom profitable work. If one wishes to examine a

solid stool, a small fragment is mixed with 1.5 c.c. of distilled water. To this is added 54 c.c. of a mixture of equal parts alcohol and ether, and it is centrifugalized for ten minutes. A smear is made from the sediment. Of course, one should test the bacillus as to its alcohol-fast as well as acid-fast properties.

In certain cases of intestinal fermentation it may be well to examine for *Bacillus bifidus*. The search of Bacillus typhosus by the use of the Drigalski-Conradi medium is seldom of practical importance in the diagnosis of typhoid fever.

CHEMICAL ANALYSIS

The chemical analysis of the stool is seldom of any practical importance in the hands of clinicians, but the detection of occult blood in the stools is a marked exception and should always be tested for in doubtful gastro-intestinal cases. Even the fresh blood accompanying a firm stool and ascribed to hemorrhoids is of importance, since there is evidence that these repeated small bleedings may lead to severe anemia. Blood in any amount from the cecal region or colon is discharged red and fluid, but blood in small quantities from even the colon, or from the small intestine, is usually mixed with the feces and can be detected only on chemical or spectroscopic examination. A great deal of interest, and rightly, is now centered on the minute traces of digested blood found in the stools in malignant disease or ulcer of the stomach. The idea is that a constant trace is suggestive of cancer, while in ulcer there are periods with much blood present and then periods with none. Since tests are also given by all hemoglobin-containing and some by chlorophyl-containing foods, and all by some medicines, the patient should be on a diet of milk, bread and eggs, the limits of which diet-period are sharply marked by charcoal. The turpentine-guaiac test is given positively by too many foods, and so the aloin test is preferred because of its delicacy and because it is not given by chlorophyl or urobilin. This test too often fails to

show blood with tuberculous ulcers of the bowel, while in chronic passive congestion blood is usually present. This test has proved of greatest value in the diagnosis of gastric carcinoma and in the differential diagnosis between ulcer of the stomach and nervous gastralgia. But in the case of gastric carcinoma I do not think it is as important as the test for blood in the gastric contents.

I believe that the bilirubin tests also have practical clinical value in the diagnosis of the location of a bowel trouble, whether in the colon alone, in which bilirubin cannot be detected in the stools or in the small bowel also, in which cases it will be formed. Schmidt's test is easy and satisfactory.

Microscope-stage chemistry is often valuable, and is easy for one practiced in that technic. One forms an idea as to the amount of muscle fibers digested, and readily distinguishes between mucus and vegetable tissue. Fatty acid crystals are seen as short, delicate curved needles which are clustered in thick masses. These are dissolved on warming and in ether. Soap may be present in yellow masses of calcium soaps, in colorless masses and in long needles in clusters or fans, or as short, plump crystals or scales. The most of the crystals one sees are soaps. Soaps are not soluble in ether but are in water. One of the best tests for soaps is to warm the stool on the slide with a drop of acetic acid and watch the crystals of fatty acid crystallize out. The droplets of neutral fat are soluble in ether and give the Sudan III test. But droplets are seldom seen unless there is a great increase in the stool. Hawes[2] has shown that an increase of visible fat under the microscope will certainly mean an increase of fat in the stool, but there may be an increase of the total fat without any visible evidence of it. An easy way to test the presence of fat in the stool is to press a portion under a cover-glass. If the portion selected be mucus or vegetable tissue the glass, when released, will spring back and

2. Hawes: Boston Med. and Surg. Jour., 1909, clx, 429.

air will rush in under the cover from all sides. If fat, the glass will stay down.

Starch granules are easily recognized by running a drop of Lugol's solution under the cover-glass.

Both pepsin and trypsin may be demonstrated in the stools in a case of diarrhea. The detection of trypsin has again recently attracted attention.

ABSTRACT OF DISCUSSION

DR. HENRY F. HEWES, Boston: Many men turn away from work on the feces because they claim the new methods of examination are so difficult. As a matter of fact, it is a very simple matter to make an examination of feces if time is taken and ordinary apparatus be at hand. It is much easier to obtain feces than it is to obtain the gastric contents. It is a common thing to have referred to me patients with intestinal trouble of a year's duration who have never had their feces examined. I think I have saved at least ten such individuals from the surgeon's knife, from an operation for appendicitis by examining the feces and finding mucus. There should be more study of the food elements and a determination of the functional conditions. A common objection to this is that it entails the giving of a test diet and patients will not take the test diet because it means from two to three days deprivation of their ordinary meals. Of course, when we want to be accurate the test diet must be used. But if the observer has much experience of feces examination he can draw his conclusions from the feces of any simple diet and need not keep to the strict test diet. For example, if a sufficient amount of fat is taken and if there is much disturbance in digestion or absorption of that fat there will be some evidences of it whatever the diet and one can judge pretty accurately whether there is a disturbance of fat digestion or absorption causing a failure of nutrition. I do not think that any difficulty in giving the test diet should stand in the way if one takes a little trouble. Take a microscope and examine the feces and learn what food has been taken; if one is familiar with the feces one can soon learn to note variations from the normal for the amount and character of the food taken in any given case. Certain methods should be used in a routine way in all cases in which there is any question, and these methods can be carried out perfectly well by the general practitioner in his office. It is easy to obtain feces and it is easy to learn without special instruction how to examine the feces and to recognize elements as they appear normally or in pathologic conditions; but the physician must stick to his work for a month or two until he familiarizes himself with the normal forces and learns to recognize abnormal elements.

DR. GEORGE DOCK, New Orleans: I have practiced the same methods for a long time and I can confirm every thing that has been said about the value and practicability of such an examination. There are one or two practical difficulties in the examination of stools that I have encountered which may be worth mentioning. As Dr. Hewes has just stated, the examinations are best made in the office; the more recent the stools the better. It is surprising how many persons can produce a stool at command. One can get a stool almost as easy as he can get a sample of urine in many cases. By placing a flat dish or a developing tray under the seat of a closet one can get a stool without urine. If the patient cannot have a stool at command give him a glycerin suppository. But in some cases stools must be sent. It is as important that the patient should be told how to prepare and send the stool as it is to tell him how to send a specimen of sputum. The ordinary method of obtaining a stool in an ordinary chamber and then decanting it is open to criticism. The stool should be brought to the physician in as natural condition as possible; the best thing to use is a so-called granite custard dish. Formerly I used a photographic developing tray, but the dish is cheaper and better and the stools can be kept fresh with a lid. Next to that is the ordinary fruit jar. Another point I wish to speak about is the great objection many have to examine stools; the general practitioner speaks of the disagreeableness of this sort of work. That is an individual's opinion of course. I have found, as a general thing, that the examination of a pathologic stool is no more disagreeable than the examination of sputum or stomach contents. An examination of a normal stool, however, is more disagreeable. The more pathologic the stool is the less repulsive is it. If one will practice examinations of stools, doing the actual work, not only will he find out much diagnostic information, but will be surprised to see how easy a matter it is and how few real technical difficulties there are.

DR. DAVID L. EDSALL, Philadelphia: A point of importance in regard to the test diet is its value in comparing one case with another; but to use the test diet as the only method of examination overlooks another very important point. What we want to know is how the patient digests the food taken in his ordinary diet; hence I think the most important thing in determining the condition of a patient so far as examining the stools is concerned, is to examine the stools when he is on his ordinary diet. It is easy in this way, as a rule, to determine whether fat, protein or carbohydrate is causing disturbance in the amount and kind of food that the individual has been taking. If we simply use the standard test diet which ordinarily differs very much from what the patient has been in the habit of taking, we often do not determine what is wrong in his manner of life. Another thing which has not been men-

tioned I have found extremely helpful, namely, observing the extent to which the stools ferment. It is easy to do this by simply keeping a stool in a closed jar at room temperature for from twelve to twenty-four hours and observing what degree of fermentation occurs, and the result often helps clearly in determining whether the symptoms of fermentation are due actually to abnormal degrees of fermentation in the bowels or whether the flatus and other similar symptoms are due to neurotic disorders of peristalis, etc. It helps also in outlining the diet and in determining the degree to which improvement is taking place. As to the question of mucus I feel positive that there is a strong tendency to make too much of this unless very abnormal amounts are present. Patients readily get terribly hipped about the presence of a small amount of mucus in the stools. Small amounts usually mean nothing except that there is some slight source of irritation and, probably, that Nature is making an effort to limit this irritation by protecting the bowel wall with mucus. One common and important cause of the persistent presence of mucus in the stools is the more or less excessive use of purgatives; many cases of so-called mucus colitis are merely purgative colitis and not a disease. In a large proportion of instances getting the patient to stop the use of purgatives by means of diet and other normal measures will cause the mucus to disappear from the stools entirely.

SIR JAMES ALEXANDER GRANT, M.D., Ottawa, Canada: I have listened with pleasure to the paper and discussion on the diagnostic importance of examining the contents of the alimentary canal. A neurotic condition has just been referred to. For nearly fifty years, since graduation at McGill University, I have carefully observed varied conditions of the alimentary canal, and years ago was convinced that a neurotic state of this canal had more to do with its troubles than is generally credited. My first effort on this subject was fully twenty years ago ("The Alimentary Canal and Human Decay, With Reference to The Neurons") and recently in the *New York Medical Journal* in a brief paper on "The Clefts of The Axis Cylinder, The Cable of the Nervous System." Prof. Walter Foster in his last great work (page 122) adverts to the axis cylinder having clefts, which have been observed during life and after death, but no reference whatever to the results of such an abnormal condition. Professor Sherrington of Manchester and McDonald of Sheffield, England, have carefully defined the saline constituents in the axis cylinder. Imperfect assimilation of food products, animal and vegetable, generates poisonous gaseous material, which acting directly on these very axis cylinder salines produces the clefts in question and hence the telling systemic results. There are troublesome digestion, inability to move about with usual activity, ordinary business duties most troublesome, the heart's action feeble and

imperfect, frequently approaching heart failure. Why all these indications of constitutional debility? They are entirely the result of defective power in the elaboration of blood, the outcome of these very clefts, so disturbing to the histogenetic process, in Nature's greatest laboratory, where the chief pabulum of life, blood, is generated. To counteract this there should be strict attention to diet, massage over the abdomen with antiseptic liquid soap for ten minutes daily and continued for two or three weeks, and after each massage application of electricity by means of a neurotone and dry electric cell for ten minutes at each application. Much benefit is also derived from application of electricity to the moistened extremities for a few moments daily, thus calling into action the terminals of the crural and sciatic nerves—to the pelvis, spinal cord and abdominal gangleonic system. Beyond a doubt electricity removes the clefts and reestablishes digestive power to a remarkable degree. We are but in the initial stage in this investigation, which I have briefly presented on the present occasion, feeling confident years can thus be added to any ordinary life in middle age entirely free from organic disease.

DR. WOODS HUTCHINSON, New York: There seems to be a healthy recognition of the limitations of modern methods of diagnosis; as yet we have not come to know just how far they can be depended on. One must consider both the sample of feces and the clinical history and, in case of doubt, the latter should dominate in our decision. One point in particular in an examination of the feces should be emphasized and that is: Of what does the feces actually consist? Two-thirds of the feces consists of the secretions of the glands of the lower half of the remaining third of bacteria intestines. The 85 and 95 per cent of the food that is properly digested does not appear in the stools. Only the 5 per cent of husks, bran, fibers, seeds, etc. No wonder we gaze perplexedly at the odoriferous mass, trying vainly this, that or the other food substance. Our surgical friends called attention to experiments made in the Columbia University laboratory two years ago on the various forms of intestinal suture and closure. They cut off and sutured the ends of a loop of the small intestines in such a way that it was still connected with its blood-vessels, but cut off from the lumen of the food canal. In four or five days this loop of intestine was found to be packed with apparently normal feces secreted by the glands in its mucous lining. A large part of the feces in a normal individual bears no distinct or definite relation to the food at all, only such parts of it as have escaped digestion. The recognition of mucus in the stools is most important, it is a secretion always abnormal in appreciable amounts and indicative of some neurotic disturbance in the individual. I have seen four patients with muco-enteritis who had been operated on for appendicitis; one

woman was about to be operated on a second time and was only saved when the surgeon saw the scar of the previous operation. Colica mucosa is an urticaria of the bowels, as asthum is an urticaria of the bronchi. Mucus in strings, flakes and spirals and the intestinal sand, so-called, may be compared with Curschmann's spirals and Leyden's crystals found in asthma. In both diseases relief is best obtained by attention to the nervous system, especially the vasomotor. Place a patient with a mucoenteritis in bed, feed liberally and leave the bowels absolutely alone, especially avoiding cathartics. and a larger percentage of these patients will recover, than if any intestinal treatment be employed.

THE WORK OF A COOPERATIVE HYDROTHERAPEUTIC ESTABLISHMENT

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In 1903 Dr. James J. Putnam and a number of other Boston physicians established a cooperative hydrotherapeutic institution under the name of the Medical Baths. Rooms were secured and equipped on the top floor of a modern office building conveniently located near the residential part of the city. The object of the enterprise was to furnish facilities for hydrotherapeutic treatments, especially those that require elaborate apparatus and skilled operators, so that all physicians in Boston and vicinity might avail themselves of these approved forms of treatment. At that time there was not a hydrotherapeutic douche apparatus or an electric light bath in the city, and the physicians who wished to have a patient given a wet-sheet rub or a carbon dioxid bath did not know where to find a man or woman familiar with the proper hydrotherapeutic technic.

At a meeting of physicians called by Dr. Putnam in October, 1903, it was decided that there was enough interest in hydrotherapy among physicians to make the plan of maintaining a self-supporting institution feasible and desirable. The institution when opened consisted of a large reception-room, five dressing-rooms, a large treatment-room, a douche-room, two toilet-rooms and two storerooms. The services of a professional decorator were secured in arranging tasteful and appropriate furnishings. Every aid to cleanliness and cheer-

fulness was introduced and the rooms were lighted from above as well as from the sides. In the large treatment-rooms yellow-stained and leaded glass was used in the windows which form nearly the entire side of the room. This shut out a dreary scene made up of chimney tops and railroad tracks and gave the effect of diffuse sunlight; the suggestion of warmth was produced even on a dark winter's day. The expense of fitting up the rooms amounted to about $2,000; and this was paid by gifts and loans from friends interested in the enterprise. Pledges amounting to $2,000 were secured to cover a possible deficit during the first year. To this guarantee fund many physicians subscribed. A complete douche apparatus and two hot-air cabinets were furnished by Dr. Putnam. The management of the establishment was in the hands of a committee composed of Dr. J. J. Putnam, E. G. Cutler and R. W. Lovett. I was made the medical director.

In his first annual report Dr. Putnam said:

With the increasing experience of our operators, there is no malady for which patients now take long journeys to distant water-cure establishments that cannot here be adequately treated. It is, moreover, unique in being a physicians' establishment, founded to promote the needs of the profession and their patients as well as the education of students and nurses as far as that is practicable, and conducted in such a manner that physicians can send their patients without fear that their relations to them will be anything but strengthened.

Nearly five years have passed since the above was written and time has demonstrated that the institution fills a real need. Furthermore, it has won the confidence of the medical community. Recently a circular letter was sent to 2,000 physicians in and about Boston asking them if they approved of our establishment and inviting criticism. Ninety-eight per cent. of those who replied wrote in commendation of the work.

PRESENT ORGANIZATION

In December, 1908, the enterprise was incorporated under the name of the "Institution for Physical Thera-

peutics." This placed it on a proper financial basis. If the institution had failed previously, or if suit had been brought against it, the committee of three physicians would have been liable for any amount. The capital stock of $10,000 is divided into four hundred non-assessable shares of $25 each. A circular letter was sent to every physician in eastern Massachusetts setting forth the purposes of the organization and inviting subscriptions for stock. The corporation is governed by a board of nineteen directors, consisting of seventeen physicians, one lawyer and one financier. The details of management are in the hands of an executive committee composed of five directors, including the president, Dr. J. J. Putnam. There is a restriction on the transfer of stock which will prevent it from passing out of the hands of physicians and will enable the corporation to purchase stock of any who wish to sell. It is the purpose of the directors to use any profits that may be realized to making improvements and in advancing physical therapy rather than in paying dividends on the stock.

Last year three more rooms were added, so that now there are accommodations for eight patients. This permits a rest in bed for several hours, if that is desirable, as it often is in connection with sedative procedures. With the smaller number of rooms it was sometimes necessary to cut short the period of rest, as the room was needed for another patient. The superintendence of the establishment is in the hands of a matron, who arranges the appointments for treatments, receives the patients, assigns the rooms and collects the fees. If the operators are negligent or if complaints are made by the patients she reports at once to the medical director.

The forenoons are given up to women patients, the afternoons to men. All treatments are by appointment. There are two chief attendants, a man and a woman, and each has an assistant. All four of the attendants were trained in an excellent school of medical gym-

RECORD OF A CASE OF SLIGHT CARDIAC INSUFFICIENCY (MR. B. E. B.)

	Before CO_2 Baths.						After CO_2 Baths.			
1908 Oct.	Pulse.	Blood-Pressure.	Temp.	HCl. c.c.	Na_2Co_3 Gm.	Duration, Min.	Pulse.	Blood-Pressure.	Remarks.	Wgt.
7	64	105	91	400	800	10	66	115	Dry rub, rest 25 minutes.	171½
9	64	105	90	500	1000	11	72	115	Dry rub, rest 25 minutes.	...
12	64	110	89	600	1200	12	64	125	Dry rub, rest 25 minutes.	...
15	72	105	88	700	1400	13	76	115	Dry rub, rest 25 minutes.	172
17	68	105	87	800	1600	14	72	110	Dry rub, rest 25 minutes.	...
28	68	120	86	900	1800	15	72	145	Dry rub, rest 25 minutes.	...
31	72	150	85	900	1800	16	72	150	Dry rub, rest 25 minutes.	171½
Nov. 5	68	130	84	700	1400	13	60	146	Dry rub, rest 25 minutes.	170
7	64	125	84	700	1400	13	44	145	Arc L. before bath 10 minutes. Dry rub, rest ½ hour.	...
14	60	125	87	800	1600	14	66	143	Arc L. before bath 10 minutes. Dry rub, rest ½ hour.	170

nastics and are skilled in mechanotherapy as well as in hydrotherapy.

No patient is treated unless he brings a prescription from a physician. A detailed record is kept by the operator of each treatment. Accompanying is the record in a case of slight cardiac insufficiency for which carbon dioxid baths were prescribed.

The chief attendant reports to the director daily the name of each new patient and the immediate effect of the treatment. The majority of treatments come under the head of stimulating or tonic procedures. These consist of a cold application to the warmed skin. If the cold procedure prescribed is not too intense for the individual's reactive powers a good reaction always results provided the treatment is properly given. If a good reaction is obtained, then the effect, so far as the attendant is concerned, is satisfactory. The following day the physician is informed that his patient has had the first treatment and a note is added in regard to the reaction. Last year when a physician referred a patient to the institution for the first time a letter like the following was sent to the doctor:

Our chief attendant reports that your patient, ————, took his first treatment yesterday at the Medical Baths and a good reaction was obtained.

We are urging all physicians who are sending patients to the baths to familiarize themselves with the details of modern hydrotherapeutic technic. No one can doubt that hydrotherapy, the most important of all the forms of physical therapy, will play as important a part in the therapeutics of the future in America as it does to-day in Germany.

If physicians accompany their patients for the first few treatments they soon gain a working knowledge of hydrotherapy, and the effect of the doctor's presence on the patient as well as on the attendant is beneficial. When patients begin a course of hydrotherapeutic treatments they are frequently apprehensive and distrustful. Those physicians have obtained the best results who have been present at one of the first treatments. They have been able to arrange or to discuss with the attendant the details of the hydrotherapeutic procedure and to observe its immediate effect. If this plan is followed it will

be found that the patients take up the course of treatments with more confidence and earnestness. This is particularly true in the case of neurasthenic patients in whom the psychic effect of the treatments is especially pronounced.

EQUIPMENT

The chief apparatus is as follows:

1. Electric light cabinet. This is an octagonal box lined with plate-glass mirrors and lighted with eight rows of six incandescent lights.
2. Two cabinets for hot-air and vapor baths.
3. Incandescent electric light bath for treating single parts of the body.
4. Arc-light with reflector for local treatments.
5. Local hot-air bath.
6. Douche-table with which a large tank for hot water and a pressure pump is connected. Temperature and pressure are completely under the operator's control.
7. Circular douche (needle-bath).
8. Rain douche (shower-bath).
9. Horizontal douche (spout).
   (a) Jet douche.
   (b) Fan douche.
10. Ascending or perineal douche.
11. Sitz-bath.
12. Porcelain tub used for
   (a) carbon dioxid baths.
   (b) electric baths.
   (c) half-baths.
   (d) full baths.
13. Electric cabinet (galvanic, faradic and sinusoidal).

FORMS OF TREATMENT

They can be divided into two classes, (1) the general and (2) the local. Most of the general treatments can in turn be separated into the stimulating and the sedative.

The immediate object of the stimulating or cold-water treatments of short duration is to produce a good reaction.[1] One understands by a reaction the secondary dilatation of the cutaneous vessels which follows their

1. The cold procedures of longer duration so valuable in combating infectious fevers are not discussed in this paper.

primary contraction produced by the stimulus of the cold water. There is an increased flow of blood through the dilated vessels, the skin reddens and there is a pleasant sensation of warmth, often accompanied by a feeling of well-being.

To promote a good reaction the skin should be warm and filled with blood before the application of the cold water. For this purpose we use chiefly electric light baths of short duration. Formerly hot-air baths were employed, but light baths are more satisfactory. In general the colder the water, the shorter its application; and the greater the force of impact on the skin, the more prompt and intense the reaction.

The mode of drying the patient and the after-treatment are important considerations in the production of a reaction. Rough towels should be used and vigorous friction applied to the body. If the individual is weak and anemic it is well after the treatment to put him to bed well rolled up in blankets and, if a reaction does not promptly develop, to place hot-water bottles at the feet and over the spine. If the patient is strong and vigorous it is advisable for him to dress without delay and take a short, brisk walk which will promote the reaction. Active measures are always better than passive, unless the patient is enfeebled. Hence, a walk after the treatment is better than massage if the condition of the patient permits.

Failure to understand the nature and significance of the reaction accounts for many mistakes in preparing hydrotherapeutic prescriptions. A measure of the reactive power of the patient can be obtained with the procedure known as the ablution with friction. This is the *Teilwaschung* of the Germans. It is the mildest general treatment, and can be employed to advantage even in the treatment of feeble, bedridden patients. The water is best applied with a wet bath mitten. One part of the body after another should be rubbed, first with cold water (50-75) and then with a rough towel. If the

circulation is poor alcohol may be added to the water. The skin of the part treated should become red and warm. The intensity of the local reaction furnishes a guide to the selection of the proper tonic measure. If a good reaction is obtained with the ablution, stronger measures may be used, of which the douches have the greatest range of usefulness. A prescription that I often give is the following:

℞.

Electric light bath for.....5 to 10 minutes
Circular douche at 105°.....30 seconds
Circular douche at 90°.....30 seconds
Jet and fan douche to entire body at 70°..20 seconds
Pressure, 10 pounds.

Repeat daily, gradually increasing pressure of jet douche and lowering terminal temperature until pressure of 20 pounds and temperature of 60° are used.

The following is a list of general stimulating treatments:[2]

1. The ablution (wet mit. friction).
2. The wet-sheet rub.
3. The half bath. Temperature, 70 to 85. Duration 1 to 5 minutes.
4. The douches:
   (a) circular douche, 60 to 70. Pressure, 8 to 15 pounds; duration, 50 to 60 minutes.
   (b) Jet and fan douche, 60 to 75. Pressure, 10 to 25 pounds.
5. The faradic electric baths. Temperature 90 to 93.
6. The carbon dioxid baths. Various strengths; temperature 85 to 92. Duration, 7 to 15 minutes.

The chief sedative treatments are as follows:

1. The wet pack.
2. The dry blanket pack.
3. The hot-air bath. Temperature, 115 to 140. Duration, 15 to 25 minutes.
4. The electric light bath. Temperature, 110 to 140. Duration, 15 to 30 minutes.
5. The neutral full bath. Temperature, 90 to 93. Duration, 10 to 45 minutes.

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2. The technic of the different procedures will be found described in detail in the excellent works of Matthes, Baruch, and Kellogg on hydrotherapy.

6. The hot full bath. Temperature, 104 to 108. Duration, 5 to 10 minutes.
7. The galvanic bath. Temperature, 90 to 93. Duration, 5 to 15 minutes.
8. The sinusoidal bath. Temperature, 90 to 93. Duration, 5 to 15 minutes.

Local treatments with heat produce hyperemia and are used chiefly to relieve pain, to lessen inflammation, and to improve the nutrition of the affected part. They are most useful in the treatment of the various joint troubles, neuralgia, neuritis and muscular affections.

1. Electric light (incandescent) bath.
2. Arc light with reflector.
3. Hot-air bath.
4. Hot-air douche.
5. Hot-water douches:
   (a) Simple hot douche.
   (b) Scotch douche.
   (c) Alternating douche.
6. Fomentations.

Of the various treatments given in the above list we use the electric-light bath, the wet mit friction, the circular and horizontal douche and the carbon dioxid bath more than all others combined. The hot-air and vapor baths are rarely employed, as their place has been taken by the electric light bath. Nearly all patients object if the hot-air bath is substituted for the light bath. The light bath of short duration usually produces the sensation of a pleasant stimulation, while a hot-air bath often gives rise to a slight feeling of oppression. Sweating occurs more quickly and at lower temperature in the light bath.

Simplicity in prescribing is well nigh as important in hydrotherapy as in pharmacotherapy. In some American sanatoriums a confusing variety of treatments are given to a single patient. This practice has all the faults of the ordinary "shotgun" prescriptions and at the end of several weeks it is impossible to decide which of the various procedures used has had a beneficial effect.

In writing prescriptions the exact temperature of the water should be stated and the exact duration of treatment. Cold water and hot water are relative terms. Tap water is commonly regarded as cold water. Yet it varies in Boston from 40 degrees in winter to 75 degrees in summer. It should be remembered that hydrotherapy is really thermotherapy, for it is the heat of the water and not the water itself that is the therapeutic agent. A full tub bath at 80 degrees, of five minutes' duration, has a tonic action, but a full tub bath of 92 degrees, of fifteen minutes' duration, has a pronounced sedative effect.

INDICATIONS OF HYDROTHERAPY

Hydrotherapeutic procedures are of value in the treatment of almost all chronic diseases. I have found them of great help in improving the general condition of patients. An increase in appetite and a better circulation of the blood in the skin and subcutaneous tissues is usually observed; and there is a beneficial action on the peripheral nervous system and increased functional activity of the skin.

The importance of hydrotherapy in anemia, in malnutrition, and in convalescence from acute diseases is not sufficiently recognized. As it can lessen pain and give a sense of physical comfort, it has a wide field of usefulness in the care of patients suffering from incurable and fatal diseases. Special emphasis should be placed on the fact that the simple physical measures can often replace the objectionable narcotics in the treatment of chronic maladies. A patient with tabes who had not had a good night's sleep for six months owing to lightning pains was able to sleep and to keep at his work an entire season with the aid of neutral and carbon dioxid baths without recourse to analgesics or narcotics.

Hydrotherapy is a most useful measure in cases of psychoneurosis that present somatic manifestations or in which the physical condition is not good. I have em-

ployed it with benefit in psychasthenia and other mental disturbances. Hydrotherapeutic measures given by skilful attendants in a well-equipped and well-conducted institution have an important psychic influence for good. This is increased by the general sense of refreshment and invigoration produced by the reaction that follows a stimulating procedure. In individuals who are not readily suggestible definite sensations of physical well-being are often necessary before there can be any improvement in the mental condition. Hope of recovery is not infrequently strengthened as a result of a good reaction, and fears and anxieties temporarily cast aside.

Cold applications exert a definite influence on the will-power, the effect of which on the psychical condition, as Brieger points out, should not be underestimated. The patient is subjected to cold stimuli, which often produce unpleasant sensations, especially at the beginning of the treatment. Sooner or later the patient realizes the beneficial action and then willingly submits to the initial feeling of discomfort. This develops increased mental stamina. Hydrotherapy should, of course, form only a part of the treatment, and other measures, such as diet, rest, isolation, exercise, work, and drugs, should be used as indicated.

The great majority of the patients sent to our institution have been affected with various forms of psychoneurosis. There have been many joint cases, not a few of which have been arthralgias of psychic origin, although most of these were mistaken for chronic rheumatism. The number of patients with arthritis, anemia, nephritis, neuralgia, neuritis and other organic diseases have been small. It is hoped that as knowledge of hydrotherapy increases among the profession it will be used more in these conditions. In Berlin during a space of less than three years 504 cases of sciatica were treated by Brieger in the hydrotherapeutic institution of the university. During the same period we treated less than half a dozen cases of sciatica in our institution, yet

there was no other place in Boston where the methods employed by Brieger were available. This means that many sufferers from the disease in Boston were denied the most approved treatment for the subacute stage.

In disturbances of psychic origin the immediate effect of the treatment on the mind of the patient can never be predicted. Sometimes there is speedy improvement, but often subjective symptoms remain unchanged or are increased after the first one or two treatments and the idea gets fixed that no benefit will result. But persistence in treatment over weeks and months often leads to great improvement or even cure in this class of cases. Success depends largely on the masterfulness of the physician in charge. Dr. Baldwin has shown that remarkably good results can be obtained in time even in severe psychoneuroses if the doctor is tactful and controls the patient with a firm hand.[3]

Many cases of neurasthenia are seen in which it is difficult to determine whether a stimulating or a gentle sedative treatment is indicated. Every patient must be studied individually, and it may take some time before the proper procedure is found. No two cases are quite the same. As George Beard truly said, "If two cases are given the same treatment from beginning to end it is probable that one of them has been improperly treated." I have sometimes followed the practice of Binswanger in giving three different treatments on three successive days. After these have been repeated once or twice the treatment which seems to the patient to be most beneficial is selected. Usually one of the procedures will be condemned and one favored. In this way the support and confidence of the patient is gained.

The following sample outline of treatment is given as a suggestion:

First Day: Electric light bath, 5 to 10 minutes, followed by wet mit friction.

3. Baldwin: The Personal Element in Prescribing Hydrotherapy, Boston Med. and Surg. Jour., 1909, clx, 468.

Second Day: Carbon dioxid bath (half full strength), 10 minutes.

Third Day: Wet pack, duration 45 minutes to 1 hour.

Repeat treatments in the same order on the fourth, fifth and sixth day.

From half an hour to an hour of physical and mental rest should follow each treatment, unless the patient is robust and with good reactive powers, when a brisk walk may be substituted. Often it is a good idea to combine rest and exercise by having the patient dress quickly, walk a certain distance and on reaching home rest in bed for thirty minutes to an hour. A good proportion of the neurasthenic patients wish to discontinue treatment after the first or second bath has been taken. In many neurasthenic women a feeling of exhaustion comes on a short time after the treatment and persists the remainder of the day. This is usually regarded both by physician and patient as evidence that the hydrotherapeutic procedure has been too strong, but, as this temporary exhaustion develops after the mildest treatments and as it almost invariably disappears after the second or third treatment, the sensation of weakness is undoubtedly due in the great majority of cases to the nervous strain of the visit to the institution. The surroundings are new and the appliances are strange and somewhat formidable in appearance. I have known even physicians to appear nervous and apprehensive when placed in the electric light cabinet for the first time. Recently I saw a patient in whom weakness and depression persisted until the sixth treatment. Since then she has felt refreshed and invigorated after the bath for the rest of the day. It was possible to prove beyond question in this instance that the weakness was of purely psychic origin because the patient felt as tired after a mild treatment (wet mit friction) as after a strong one (circular and horizontal douche).

For patients who cannot afford daily treatment at our institution I prescribe three treatments a week at the Medical Baths and a home treatment in the form of a

neutral bath, or half bath, on the other days. It is well to have the home treatment taken at the same hour as that at the institution.

After considerable experience with carbon dioxid baths in the treatment of cardiac insufficiency I can only say that they have seemed to be decidedly beneficial in certain cases. The carbon dioxid baths raise the blood-pressure and produce in some instances a transitory reduction of cardiac dilatation. Often I have failed to note any improvement, and never when the heart muscle was markedly weakened. In the cardiac neuroses they are of undoubted value. Care must be exercised to select a bath of proper strength. Weak hearts are frequently overtaxed by strong baths. I have observed cases in which the congestion-dilatation of the heart was distinctly increased by the bath. If there is a fall in the blood-pressure after the bath (temperature 87 to 92 F.) it indicates that the heart is weak and the bath too strong. We usually begin the treatment with a bath one-fifth or three-tenths full strength.[4] The attendants take the blood-pressure before and after every carbon dioxid bath. I have found that the action of baths of different strength on the blood-pressure furnishes a useful method for determining the functional power of the heart muscle.

INFLUENCE OF THE INSTITUTION IN ADVANCING PHYSICAL THERAPEUTICS

The facilities of the Boston establishment have been utilized at different times during the past five years by about 200 physicians in the treatment of their patients.

Since the opening of this institution several Boston hospitals have installed hydrotherapeutic equipments. Several skilled attendants employed in local hospitals were trained in the technic of water treatments at our institution.

4. Detailed directions for preparing the baths are given in Matthes' Lehrbuch der klinischen Hydrotherapie, Edition 2, Jena, 1903, and in Romberg's Lehrbuch der Krankheiten des Herzens, Stuttgart, 1906.

Demonstrations in hydrotherapy have been given to students of the different medical schools in this city.

Our organization, cooperating with local medical societies, has secured several addresses by prominent physicians on hydrotherapy and other forms of physical therapeutics.

Reprints of articles on hydrotherapy have been sent to over 2,000 physicians in eastern Massachusetts.

The institution has been visited by physicians from many parts of the country and establishments patterned in a measure after ours have been started in other places.

313 Beacon Street.

ABSTRACT OF DISCUSSION

DR. JOHN A. LICHTY, Pittsburg, Pa.: Such an institution as described by Dr. Pratt is, I think, a necessary adjunct to the physician's armamentarium. If the physicians do not become active and take up this matter, the quacks will, and with great harm to the patients. All of us no doubt have had the same experience. I have in mind one patient with loss of cardiac compensation, enlarged liver, etc., who went to an ordinary masseur, or a man who called himself "professor of hydrotherapy" to have his enlarged liver reduced in size. The massage and exercises prescribed led to serious results. This I have seen frequently, and I believe we should protect ourselves against these men. Unless we establish such institutions, we will be at the mercy of these men. The difficulties mentioned I believe to be the difficulties one would expect naturally in trying to treat ambulatory patients. It is difficult to prescribe a treatment to be taken in the patient's home. If the patient will go to a hydropathic institution, he will go to the physician's office. If a woman is to take the treatment, she dresses, goes down the street, takes the treatment and then goes to a department store to do her shopping. The good that follows the carrying out of such a course, under such difficulties, is small. In Pittsburg, such an institution is about to be opened, and I think we shall get good results from it. If we could send patients to Boston and have them devote the time necessary for the treatment in Dr. Pratt's institution, I know good results will follow; I also believe that if those patients who were not much benefited at his institution in Boston, were sent to a similar institution at Pittsburg, away from their home and environment, in all probability good results would follow. These patients take the treatment much better in institutions devoted to that purpose. In this coun-

try the watering-places and institutions are not manned as in other countries. Some of the best scientific work originates in some of these establishments in Europe. Good men are there to watch their patients carefully and prescribe the treatment to be employed. There are very few institutions in this country where the patients can be so treated; what is being done in this line, however, is being appreciated. At these watering-places the patients can enjoy themselves. The treatment in this country is a business; there is no amusement, no enjoyment for the patients in the institutions we have here. It is different in the watering-places in Europe. One advantage that is coming from the establishment of these institutions is the education of helpers so that the treatment may be carried out in the patient's own home. I am sorry Dr. Babcock is not here to tell of the Nauheim treatment as he has it carried out in the patient's own home. Nauheim himself has stated that it cannot be done at home; but Dr. Babcock has proved that it can be done and with very satisfactory results when the conditions can be entirely controlled.

DR. G. C. SMITH, Boston: Dr. Pratt's work in Boston is well known throughout the New England States, and especially in Massachusetts, while in the South and West people have heard much less about it.

One or two points suggested by the paper I would like to touch on. There is a class of cases in which I have found hydrotherapy especially adapted, namely, vasomotor conditions with a neurotic etiology; also vasomotor conditions arising from a failing heart in cardiac disease, a condition so often seen in young boys and girls. These conditions are quickly relieved by hydrotherapeutic measures. Often patients who have been very little benefited by drug treatment can be satisfactorily treated by good sanitary measures, open-air life, proper diet and hydrotherapy, and show rapid improvement under such conditions. Other patients who do much better in America than abroad are the patients with broken compensation. This is my opinion after a study of the institutions abroad. The reason is that the physician knows the patient and is interested in him; he knows all the individual's idiosyncrasies. At Nauheim or other sanitaria abroad the patient is treated more largely from a cardiac standpoint which does not always work out well. I have had many patients try the Nauheim treatment, and they still continue to try it. They go abroad and spend from four to six weeks, and sometimes it is claimed that the transverse cardiac dulness has been reduced two inches in that time. That is absurd. The only way to do away with the stupendous outflow of the misinformed and misled from this country is to let the real facts be known. I know of several individuals in Boston who have been treated at Nauheim and other spas abroad who now make it a regular thing to consult the family physician in Boston and have

a thorough examination before going. On their return they do the same thing. In these patients we cannot find the same diminution in the cardiac dulness as the foreign physicians claim. I am sure that hydrotherapy does help these patients. It must be remembered that many patients who have cardiac disease must be treated at home, and that this number is much greater than the number going abroad.

DR. ANDREW MACFARLANE, Albany, N. Y.: The first duty of the physician is to cure his patient, and there is no question that the true way to do this is to find out the cause of his difficulty and remove it. This, however, does not appeal to the popular mind. Consider what has been done to stop the spread of smallpox by vaccination and to prevent typhoid fever by a pure water supply; the citation of such facts, however, does not present an argument to the average popular mind that will have any marked influence. If a patient with a stiff joint consults physicians, they are likely to give him pills, solutions, powders and liniments and often without much effect. The patient then goes two or three times to an osteopath, gets as many treatments and is benefited. He then is convinced that the osteopath is a better physician than the regular practitioner. He certainly is to that extent. The great mistake is that the medical profession does not appreciate the value of physical therapy. Physicians rely too much on giving prescriptions and then sending the patient home.

In New York State there is a man who conducts a successful sanatorium; he is an ex-prize fighter. Yet his place is frequented not by the ignorant, but by the most intelligent men in the United States. I regard it as a disgrace to the entire medical profession that an ex-prize fighter should be able to do, and to do successfully, what a scientific profession is not doing. In our various efforts to secure proper legislation in New York State we had the greatest possible difficulty in proving that the so-called regular medicine was better than fake medicine.

After taking the baths at the foreign spas the patients rest. I have visited many spas in Germany and I am fairly well acquainted with the conditions existing there. The Germans have developed the scientific side of metabolism in these watering-places to an extent which we would do well to copy and imitate.

I believe that the subject that Dr. Pratt has brought up is a most valuable one, and I have no doubt but that great advances will be noted in it during the next fifteen or twenty years; but we must not expect much from it in three, four or five years. This is, however, a subject that will bear much and good fruit in time.

DR. JOSEPH H. PRATT, Boston: It is true that many patients with neurasthenia and other forms of psychoneurosis can receive better treatment in a suitable sanatorium than at home,

but sanatorium treatment is frequently out of the question owing to the expense. Boston physicians have been gratified at the good results obtained by home treatment combined with systematic hydrotherapy in their local institution. In addition to the hydrotherapeutic treatment itself, the daily visit to the baths, the association with a kindly and cheerful attendant or nurse, the half-hour or hour of rest before dressing, often have a marked influence for good on both mind and body. Furthermore, the institution is an aid to the physician in his supervision of the case. If a patient is told to take a treatment at a certain hour daily in our establishment, it is an easy matter to find out whether he does so or not. A report is sent to the physicians, if requested, of the number of treatments taken by each patient and the date of each treatment.

In the management of patients with chronic organic disease, treatments at the medical baths have been of aid in encouraging the patients to persevere in following an unpleasant or exacting regimen. This is true in cases of nephritis, obesity, diabetes and heart disease. In 1905 I saw with Dr. Daniel a woman with chronic nephritis who had been ill a year. She had marked general anasarca and the day urine contained over 1 per cent. of albumin. The essential features of the treatment instituted were electric-light baths and a salt-free diet. She objected strongly to the diet, but did not abandon the plan of treatment because she felt that the light baths were beneficial. After three months the edema had disappeared except for a slight swelling of the legs. When last seen, three years later, the edema had not recurred and the urine contained only a slight trace of albumin. It is probable that her recovery was due more to the salt-free diet than to the light baths, yet without them she never would have continued with the diet.

It is strange that American physicians who send patients to Nauheim make so little use of artificial carbondioxid baths. Krehl, Romberg and other German authorities recommend and employ in their clinics the artificial baths. There are over a dozen natural carbon-dioxid baths in Germany used in the treatment of heart disease in addition to those at Nauheim. Two patients with cardiac disease whom I referred to a leading German consultant were sent not to Nauheim, but to Homburg. What I have learned from patients returned from Nauheim bears out Dr. Smith's statement. Treatments are often given there with inadequate supervision.

There is need of a thorough and unprejudiced investigation of the effects and value of carbon-dioxid baths, and this can well be carried out in establishments like the one described.

CLINICAL VALUE OF RECENT STUDIES IN EXPERIMENTAL NEPHRITIS

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A symposium on nephritis at the present time quite fittingly is opened with a reference to the results of recent work in experimental nephritis. This, however, is not the case so much because the results as yet are of very great importance, but rather because it seems likely that the experimental method applied to the study of nephritis will in the future throw much light on the problems of the disease.

The history of the study of nephritis is not long. With Bright in 1827 begins our accurate knowledge. He it was who linked together in causal relation the symptoms, albuminuria and edema, and the lesions in the kidney. Keen observers added fact after fact for fifty years and more. Technical improvements widened the field of observation, so that a period, which we may arbitrarily end in the early part of the present decade, had contributed much to our knowledge of nephritis through the work of pathologists and clinicians. Yet our knowledge remained largely a knowledge of results rather than a knowledge of causes and progressive development, and many were the gaps in our knowledge, great the discrepancies between clinical observation and postmortem finding. In the present decade the experimental method has been applied increasingly in the study of disease in the hope that by it our knowledge of the life-history and causes of disease might be extended.

Nephritis has been studied in this way and certain results have been obtained.[1]

I am not asked to review the numerous experimental studies of nephritis that have been published in recent years, but to indicate what clinical bearing, if any, this work has. If we turn to nephritis in man, we find the following phases of the disease of much clinical interest: the urinary changes, particularly the albuminuria and cylindruria, the uremia, the edema, the hypertension and associated cardiac hypertrophy, and, finally, the cause and the cure. Do our studies of experimental nephritis help in a better understanding of any of these? To answer this I will consider these points in the order named.

URINARY CHANGES

There has been a very general consensus of opinion with regard to albuminuria in nephritis. The albumin of the urine, in very large proportion, comes from the soluble proteids of the circulating blood and appears in the urine as a result of a pathologically increased permeability of the glomerular tuft. Degeneration of the epithelial cells of the tubules may have a small part in producing the condition. Experimental work confirms this view.

Cylindruria has received two interpretations. One of these assumes that the albuminous material constituting the cast arises from the albumin of the blood, which, after excretion through the injured glomerulus, becomes changed in physical properties so as to fuse together into a homogeneous coagulated mass, a cast. The other theory assumes that the albuminous material of the cast is derived from the albuminous material of the epithelium lining the tubules, which becomes fused together and more or less homogeneous so as to make up a cast. This latter theory does not assume that there has been any very great change in the physical composition

1. Christian: Experimental Nephritis (a review of recent literature), Boston Med. and Surg. Jour., 1908, clviii, 416, 452.

of the albuminous material between its cell origin and the cast, since cells and casts present in the urine show many identical physical properties.

The origin of urinary casts has been studied in nephritis produced experimentally. A variety of irritants, such as cantharidin, corrosive sublimate, uranium nitrate, potassium bichromate, etc., when given to animals, will produce changes in the kidney leading to the appearance of albumin and casts in the urine. Wallerstein,[2] among others, has conducted such experiments and concludes that all casts are formed from degenerated, disintegrated and metamorphosed tubular epithelium. Ribbert[3] and Schlecht,[4] on the other hand, studying the excretion of carmine through the kidney, have concluded that the hyaline casts are derived from the albumin excreted through the glomeruli, while the granular casts are derived from tubular epithelium.

In our laboratory at Harvard this subject has been investigated by Dr. R. M. Smith,[5] who employed rabbits and used a variety of irritants. Roughly, the irritants used may be divided into two groups: those which produce extensive changes of a degenerative character in the tubular epithelium (uranium nitrate, potassium bichromate and mercuric chlorid), and those which, while producing evidence of acute nephritis, produce comparatively slight changes in the tubular epithelium (cantharidin and arsenic). By varying the size of the dose of these irritants, by varying the number of doses, by varying the time interval between the doses, by varying the length of the experiment, which ends either in the spontaneous death of the animal or in killing the animal, it is possible very largely to control the lesions,

2. Wallerstein: Experimentelle Untersuchungen über der Entstehung der Harnzylinder, Ztschr. f. klin. Med., 1906, lviii, 296.

3. Ribbert: Die Abscheidung intravenös injiziertes gelösten Karmins in den Geweben, Ztschr. f. allg. Physiol., 1904, iv, 201.

4. Schlecht: Experimentelle Untersuchungen über der Resorption und der Ausscheidung des Lithionskarmins, etc., Beitr. z. Path. Anat., etc. (Ziegler's), 1907, xl, 312.

5. Smith: The Origin of Urinary Casts; an Experimental Study, Boston Med. and Surg. Jour., 1908, clviii, 354.

and in this way there comes a manifest advantage in the experimental method as compared with a study of post-mortem lesions in man.

It was found in this work that the irritants which produced marked degenerative changes in the epithelium of the tubules gave rise to a more abundant cast formation than did the other group of irritants. The urine of the animals employed, rabbits, was collected and the number and character of the casts was studied from time to time. By those irritants which produce most marked degenerative changes of the epithelium of the tubules most casts are produced, indicating that there is a close association between changes in the epithelium of the tubules and cast formation. By studying histologically kidneys of animals receiving different irritants in varying dosage, cast formation could be traced morphologically. The first change seems to be a granular degeneration of the epithelium lining the distal convoluted tubules, which increases in severity until the epithelium becomes converted into a granular material more or less completely filling the space bounded by the basement membrane of the tubule. This granular material is composed of remains of both cytoplasm and nuclear material. While this process is going on, fluid is presumably excreted through the glomerulus, so that there is a current of excreted fluid along the tubules which washes this granular material into the lower levels of the tubules. Toxic substances used in this way cause very slight degenerative changes in the epithelium lining the collecting tubules, and so the granular material washed down in the collecting tubules comes in contact with quite normal epithelium. In this process of passing along the tubule the granular material seems to become fused into plugs molded by the shape of the collecting tubule, and by the time the mass reaches the hilum of the kidney it is a well-fused granular plug, which floats out into the urine as a granular cast.

In the earlier stages of the process, urine analysis shows the presence of a number of casts, at first coarsely granular, later more finely granular. With a longer interval, or with a less intense local process, urine analysis shows casts more hyaline in character, and the sections from the corresponding kidneys show that in the lower levels of the tubules there are present plugs varying in homogeneity, and always in the older processes being quite distinctly hyaline. Even in the very chronic lesions, application of appropriate staining methods shows in these very homogeneous, hyaline, highly refractile casts the presence of numerous granules staining in every way identically with the granules that are in renal epithelium. So that from a morphologic point of view, supported by the results of urinary analysis, it would seem that both granular and hyaline casts in these animals arise from degenerative processes in the epithelium, and that the granular casts come early, the hyaline casts late, that there is a progressive transformation between granular and hyaline casts, and that granular casts appear to be formed quickly and excreted early, while hyaline casts are formed slowly and excreted late. These observations on animals are in harmony with the observed conditions in man, and would satisfactorily explain cast formation in most cases, though possibly not in every case.

Cast showers are occasionally observed in man. Experimental study has given some explanation of this. In Mackenzie's laboratory in Toronto[6] it has been found that in experimental nephritis, if, at a time after the casts have very largely ceased to appear in the urine, the renal artery is dissected out and physiologic salt solution is irrigated through the kidney under some pressure, a certain amount of fluid will be excreted through the ureter, and this will be found to contain a very large number of casts, largely hyaline in character. It

6. Unpublished Experiments Reported by Mackenzie at the Meetin of the American Association of Pathologists and Bacteriologists, held in Boston, April 9 and 10, 1909.

would seem that, with a cessation of the active process, casts that have been formed have remained stored in parts of the tubules and gradually become hyaline in character; with increased flow of fluid through the renal vessels these will be washed out in large numbers. A similar acceleration of renal circulation with accompanying diuresis would in man similarly flush out a large number of casts and produce cast showers.

UREMIA

A number of theories have been advanced to explain the condition of uremia. Most of these assume the presence in the body of the nephritic of some toxic substance which, accumulating up to a certain point, produces the symptoms which we know as uremia. Attempt has been made experimentally to produce a similar condition in animals by means of nephrectomy, by ligation of the ureters, and by the administration of various irritants. In this way toxic conditions undoubtedly are produced which have some analogy to uremia in man, but the recognition in animals of symptoms, which may be regarded as truly uremic in the sense of this condition in man, is so exceedingly difficult that at the present time no great advance has been made, and it cannot be said that studies of experimental nephritis have thrown much light on the condition of uremia beyond giving support to the view that the condition is a toxic one associated with renal lesion.

EDEMA

From the earliest period of the work on nephritis the relation of edema to nephritis has been the subject of much discussion and investigation. The attempt of morphologists to correlate edema with certain types of renal lesion has been only very partially successful, and morphologic studies have yielded no explanation of the occurrence of edema. In recent years physicochemical methods have been applied and especial em-

phasis has been placed on salt retention with corresponding changes in osmotic tension. Analyses of food intake and urine output with respect to sodium chlorid seemed to show that in cases of nephritis with edema there was a deficient salt excretion and that the edema fluctuated in proportion to the salt intake. Widal and a group of French observers[7] have placed particular emphasis on salt-free diet as a means of controlling nephritic edema. A critical review[8] of the whole subject of the salt retention theory, however, seems to show that it is insufficiently supported. A considerable amount of experimental work is rather against it. Acute toxic nephritis in which there is no hydrops can be produced by various substances, and in these animals salt retention may take place. On the other hand, with uranium nitrate nephritis is produced in which edema is often present without there being any more salt retention than occurs in other types of toxic nephritis without edema. Recent careful clinical studies of Bittorf[9] and of Blooker[10] have failed to show any close relation between salt retention and edema. Renal cases without edema may exhibit a marked decrease in power to excrete ingested salt.[11] There is then undoubtedly a growing skepticism toward salt retention as a primal cause of nephritic edema, though in many cases it may be a contributing factor,

7. Widal: La cure de déchloruration, Bull. et mém. Soc. méd. d. hôp. de Paris, 1903, xx, 990.
Widal, Froin and Digne: La chloruration et la régime dé chloruré ches les cardiaques, Soc. méd. d. hôp. de Paris, 1903, xx, 1208.
Widal and Javal: La cure de déchloruration; son action à certaines périodes de la néphrite épithéliale, Bull. et mém. Soc. méd. d. hôp., 1903, xx, 733.
Widal and Lemierre: Pathogénie de certains œdémes brightiques; action du chlorure de sodium ingéré, Bull. et mém. Soc. méd. d. hôp., 1903, xx, 678, 785.
Widal and Others: Les régimes déchlorurés, Eighth French Cong. Int. med., Liege, Sept. 25-27, 1905, Sem. méd., 1905, xxv, 469.

8. Georgopulos: Experimentelle Beiträge zur Frage des Nierenwassersucht, Ztschr. f. klin. Med., 1906, xl, 411, and other similar papers.

9. Bittorf: Zur Pathologie des Wasserund Salzstoffwechsels, Deutsch. Arch. f. klin. Med., 1908, xciv, 84.

10. Blooker: Ueber den Einfluss der Kochsalzzufuhr auf die nephritischen Oedeme, Deutsch. Arch. f. klin. Med., 1909, xcvi, 80.

11. Ambard and Beaujard: La rétention chlorurée sèche, Semaine méd., 1905, xxv, 133; and other observers.

and the withholding of salt from the food may be therapeutically effective. Many failures from this form of treatment, however, show its limited applicability.

On the other hand, there is increasing evidence to show that peripheral vascular lesions play a large rôle in the production of edema. This is not a new theory, but was advanced in 1877 by Cohnheim and Lichtheim[12] and more recently has been supported by Senator. It presupposes the presence in the circulating blood of some toxic substance capable of injuring the vessel wall. Some evidence of the existence of such a toxic substance is found in the experiments of Heineke,[13] Meyerstein[14] and Blanck.[15] These experiments were as follows: It is known that subcutaneous injections of uranium nitrate in rabbits will produce a toxic nephritis usually with edema, whereas other substances may be used to produce nephritic changes without any associated edema. Now if blood serum obtained from rabbits of the first group be injected into rabbits of the second group, edema appears, whereas normal rabbit serum produces no such result. Experiments of this kind are not constant in their results, but at least they are very suggestive of the importance of the rôle of circulating toxic substances in producing nephritic edema.

Pearce[16] has recently added further evidence in favor of the rôle of peripheral vascular lesions in the production of edema by a group of experiments in which he used known renal irritants and substances which are known to produce degenerative changes in the blood-vessels. Snake venom is such a vascular poison, and

12. Cohnheim and Lichtheim: Ueber Hydrämie und hydrämische Oedeme, Virchows Arch. f. path. Anat., 1877, lxix, 106.

13. Heineke: Diskussion, Verhandl. d. deutsch. path. Gesellsch., 1905, ix, 107.

14. Heineke und Meyerstein: Experimentelle Untersuchungen über den Hydrops bei Nierenkrankheiten, Deutsch. Arch. f. klin. Med., 1907, xc, 101.

15. Blanck: Experimentelle Beiträge zur Pathogenese der Nierenwassersucht, Ztschr. f. klin. Med., 1906, lx, 472.

16. Pearce: The Theory of Chemical Correlation as Applied to the Pathology of the Kidney, Arch. Int. Med., 1908, ii, 77; and unpublished experiments reported at the meeting of the American Association of Pathologists and Bacteriologists, held in Boston, April, 9 and 10, 1909.

when given in association with a renal irritant edema results in a considerable proportion of the animals, particularly when moderately increased amounts of water are given by mouth, whereas the same treatment without the use of the vascular poison rarely results in edema. The functional studies of Schlayer, Hedinger and Takayasu[17] show that there is a close relation between the functional renal vascular disturbance and the edema.

Further evidence in support of the part played by vascular lesions in the production of nephritic edema is given by the results of my own histologic studies,[18] in which, in an examination of the kidneys of rabbits after the use of various renal irritants, I have found quite constantly associated with uranium nitrate lesions a change in the walls of the vessels of the glomerular tuft, consisting of the appearance in them of numerous hyaline droplets demonstrable by special staining methods. This vascular lesion was not found in kidneys of animals receiving substances other than uranium nitrate, and, as the uranium nitrate is the substance which produces in rabbits edema much more constantly than any other substance, it may be inferred that there is some relation between this anatomic lesion and the occurrence of the edema.

It cannot be claimed that the evidence is complete, but so far as the results of experimental work go it is very strongly suggested that the edema in nephritis results from injury to the peripheral vessels associated with changes within the kidney, probably in large part vascular also. Accepting this evidence, it is not surprising that there is no strict correspondence between the occurrence of edema in man and a definite type of anatomic lesion in the kidney. It is conceivable that various anatomic lesions under certain circumstances

17. Schlayer, Hedinger and Takayasu: Ueber nephritische Oedeme, Deutsch. Arch. f. klin. Med., 1907, xci, 59.
18. Christian: A Glomerular Lesion of Experimental Nephritis, Boston Med. and Surg. Jour., 1908, clix, 8.

might lead to the production of functional disturbances in the kidney resulting in the retention or formation of toxic substances, which would injure the vascular apparatus and lead to edema formation, or it is possible that the same toxic substance which produces the renal lesion also is the cause of the vascular lesion. Much more experimental work, however, is necessary finally to determine the cause of edema.

HYPERTENSION AND ASSOCIATED CARDIAC HYPERTROPHY

Chronic nephritis is generally recognized as one of the common causes of high blood-pressure and associated cardiac hypertrophy, and a number of theories have been advanced in explanation of this condition. Some of these have been submitted to experimental test. Pässler and Heineke[19] have found that there is an increased blood-pressure and cardiac hypertrophy following the removal of considerable portions of the kidney substance, though these results were not constant. Janeway[20] has obtained similar results, though it is not very clear in just what way the blood-pressure is raised. Another group of observers have believed that the internal secretion of the kidney was a factor in raising the blood-pressure, and adduced in favor of this the fact that injections of extracts of kidney produced a rise in blood-pressure. A critical review of this work has been made by Pearce[16, 21] with additional experiments of his own, and he finds that results are very inconstant, and that the extract of the kidney of one animal may act in just the opposite way to the extract of the kidney of another species; consequently it is not believed that internal secretion in this sense can play very much part in producing hypertension. In the blood serum of animals

19. Pässler und Heineke: Versuche zur Pathologie des Morbus Brightii, Verhandl. d. deutsch. path. Gesellsch., 1905, ix, 99.

20. Janeway: Unpublished experiments reported at the Meeting of the American Society for the Advancement of Clinical Investigation, held in Washington, May 10, 1909.

21. Pearce: An Experimental Study of the Influence of Kidney Extracts and of the Serum of Animals with Renal Lesions on the Blood-Pressure, Jour. Exper. Med., 1909, xi, 430.

receiving doses of certain substances that produce renal change there may be particular substances which have a pressor action. However, this type of work experimentally so far has been confined to acute conditions, though in man suffering from chronic nephritis numerous reports have been made indicating that there are substances in the circulating blood capable of acting to raise blood-pressure, but here again more recent reports give conflicting results, and probably not a very great amount of importance can be attached at the present time to these as factors in causing hypertension.

In a certain number of experiments in which the successful production of chronic renal lesions[22] has been attained, there is evidence of cardiac hypertrophy, and further studies along this line may yield results of importance. Since at the present time we have several experimental ways of producing cardiac hypertrophy, it may be possible to unravel the cause of this condition in nephritis. As shown by Fleisher and Loeb,[23] spartein and adrenalin chlorid will lead to the production of myocarditis with cardiac hypertrophy, and a moderate number of experiments in our laboratory have shown that the myocardial lesion in this condition as well as the findings in the kidney are quite different from those in a few animals where a type of chronic experimental nephritis has resulted from repeated injections of uranium nitrate, and in neither one of these groups of animals do we find the type of vascular lesion that Klotz[24] has obtained in Montreal by his method of increasing intravascular tension by inverting rabbits, from which procedure a marked degree of arterial change with dilatation of vessels is developed in the arteries of the

22. Christian: Unpublished and incompleted experiments made in the Laboratory of the Department of the Theory and Practice of Physic at Harvard Medical School.

23. Fleisher and Loeb: Experimental Myocarditis, Arch. Int. Med., 1909, iii, 78.

24. Klotz: Experimentelle Arbeiten; Arteriosklerose, Centralbl. f. allg. Path. u. path. Anat., 1908, xix, 535.

anterior half of the body, associated with cardiac hypertrophy. Since these various experiments suggest that we can experimentally control the production of cardiac hypertrophy and obtain the result by producing chronic renal lesions, chronic myocardial lesions and chronic vascular lesions, it may be possible by such studies to arrive at the causal factor chiefly acting in any one of these types.

CAUSE AND CURE

As yet too little work has been done for the studies in experimental nephritis to throw much light on the etiology and treatment of nephritis. It is in the chronic nephritis that least is known about cause and cure. Experimental results in the production of chronic nephritis have been inconstant, and by nature such experiments are difficult. The repeated injection of various irritants has resulted in a certain number of cases in the production of lesions fairly analogous to the chronic renal lesions that we find in man. In animals, however, the remarkable recuperative power of the kidney makes the production of chronic lesions very difficult. Still, so far as results have been obtained, they suggest that in many cases chronic lesions in man result from continued action of small amounts of toxic substances, but throw no light on the cause of the appearance of these substances. Lead salts are about the only substances used experimentally which could in any possible way be similarly active in man, and it is not conceivable that lead-poisoning is a factor in the production of many cases of chronic nephritis. Some experiments seem to show that a single very extensive degenerative process in the kidney may result in the production of chronic lesions; and it may be that a few cases in man result in this way, just as at present it is believed that certain cases of cirrhosis of the liver are the result of some single acute degenerative process. Very little light so far has been thrown on the etiology of nephritis by experi-

mental methods, however, and no assistance in the cure and prevention has been given.

It is evident from this review of experimental nephritis that the work has been just begun. It is being carried on at the present time in many laboratories, and we should take courage in the belief that from these experiments much of direct clinical value will come, and that by it our knowledge of nephritis in man will eventually be considerably widened.

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THE CAUSES OF HYPERTENSION IN NEPHRITIS

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Of the causes of hypertension in nephritis we have no exact knowledge. The theories which have been elaborated are based mainly on deductions from clinical experience or to a slight extent on experiment. Neither the clinical experience nor the experimental evidence is at all conclusive; but each in its way points to an explanation through the action of some chemical substance influencing the circulatory system. What this substance is and how it acts we do not know.

Clinically we have the very important observation that hypertension and heart hypertrophy come in that group of renal diseases in which uremia is also prone to occur, while both fail in practically all other forms, as tuberculosis, pyonephrosis, hydronephrosis, cystic kidney and the kidney of acute sepsis. In other words, hypertension, like uremia, is an evidence of renal insufficiency. It is naturally suggested that the poison of uremia is identical with that causing hypertension, or, if different, is formed at the same time and due to the same causes; or possibly one is a derivative of the other as the result of some process of chemical disintegration. If the same poison, it is possible to conceive that in small amounts it affects the vasomotor apparatus (hypertension) and in large amounts exerts a toxic effect on the nervous system (uremia). Or, if two or more poisons are concerned, each may have special affinities.

In support of this chemical theory we have the frequent clinical experience that the degree of the uremic manifestations (headache, vomiting, unconsciousness) and the recovery from these have a close relation to the blood-pressure. Moreover, true uremia without hypertension seldom occurs.

In connection with this chemical theory or retention theory, the effect of diet also is suggestive. Experiments on patients with chronic nephritis have shown that rich protein diet increases tension and disturbs the general condition of the patient for the worse. Müller describes an individual in whom a change from milk and carbohydrate diet to rich meat diet caused pressure to rise from 140 to 190. Rich meat diet causes, in nephritics, headache, one of the earlest and most constant symptoms of uremia, and one which has a definite relation to hypertension.

All this probably means a retention of the products of nitrogenous metabolism, and possibly of that nitrogen which in the urinary partition is known as "rest" or undetermined nitrogen. The increase of these substances in the blood of that group of renal diseases in which uremia occurs suggests that not only may they be the cause of uremia, but that among them may also be the substances responsible for the increased tension. Aside from this theory, which attempts to explain clinical observation, we can at present add nothing to the view that hypertension is to be explained by retained products of metabolism.

Another view, which I think we can dismiss briefly, is that of the internal secretion of the kidney. This is based on Tigerstedt's observations that extracts of rabbit's kidneys contain a pressor substance, which substance Forlarini and Riva-Rocci consider may be increased in diseased kidneys. Little evidence has been brought forth to support this theory, and the most recent study, that of Pearce, was entirely negative in its results.

Another closely related theory is that which assumes a correlation between the kidney of chronic interstitial nephritis and the secretion of the adrenal. This theory was advanced by French investigators, led by Vaquez, three or four years ago. They describe a localized or diffuse hyperplasia of the adrenal accompanying chronic nephritis in those cases which do not run too rapid a course. This hyperplasia is considered as an indication of the hyperactivity of the functions of the gland; that is, essentially a condition of hyperadrenalism. Naturally the theory has a relation also to the arteriosclerosis associated so constantly with the interstitial type of nephritis. Although the correspondence between the renal lesion and the hyperplasia of the adrenalin is very suggestive and the occurrence not infrequent, there is some doubt as to the interpretation. Several German investigators, and in this country, Pearce, ascribe the anatomic changes in the adrenal, in part at least, to the influence of the local nutritional disturbances caused by local arteriosclerosis. As reports multiply, and the lesions are found in other conditions than "contracted" kidney, the importance of the observation diminishes.

Of interest in connection with the theory just described are the attempts to demonstrate adrenalin or adrenalin-like substances in the serum of nephritics. This work is based on Meltzer's observation that adrenalin causes dilatation of the pupil of the frog's eye. According to Ehrmann, the method is sufficiently delicate for the detection of adrenalin in dilution of 1 to 1,000,000. Clinically the method is associated with the names of Schur and Wiesel, who found that the serum of patients with chronic nephritis caused almost uniformly mydriasis of the enucleated frog's eye. The serum of normal individuals and of individuals suffering from other diseases failed to produce the same results. Several observers have confirmed these results, but there is some dispute as to whether or not the action is due to adrenalin. That it is, is denied by Schlayer, on the basis of his work

with the "vessel-strip" method, which gives positive results with normal serums and no different results with nephritic serums. Be this as it may, no explanation of the presence of the mydriatic body is at hand unless it be that of the French investigators and that, we have seen, is hardly satisfactory. More evidence must accumulate before a definite opinion as to the value of these observations can be reached.

As is well known, the chief difficulty in explaining hypertension in chronic interstitial nephritis is the almost constant presence of arteriosclerosis. The absence of definite knowledge of the sequence of events makes the problem a complicated one. It is still a question whether the kidney injury is primary and leads to arteriosclerosis as the result of a hypertension of renal origin, or whether a poison first affects the blood-vessels, and the kidney secondarily through the disease of its own arteries. The latter view appears to be the one gaining adherents, but it is well to remember in this connection that many poisons may simultaneously affect the kidneys and the vascular system.

On this general subject some light has been thrown as the result of the study of renal diseases following infectious diseases, in which hypertension appears to be primary and the heart hypertrophy and arteriosclerosis secondary. The hypertension associated with the glomerulonephritis of scarlet fever is of peculiar interest. Usually one thinks of hypertension coming on gradually in the course of a chronic disease, but in scarlatinal nephritis it may develop very early (Mahomed and Müller); indeed, in the course of a few days. Here certainly heart hypertrophy or arteriosclerosis can be ruled out, for in scarlet fever four weeks at least are necessary for hypertrophy (Müller) and the scarlet fever age is not that of arteriosclerosis. For such an early hypertension the only explanation which can be offered is increased peripheral resistance—a contraction of arterial terminals—as the result of some chemical in-

fluence; but this brings us again to the theories discussed above, concerning which we could come to no definite conclusion.

The frequency of the association of glomerular lesions with hypertension is of considerable interest. Schmidt, working with Krehl's material, has emphasized this relation and A. Loeb holds that heart hypertrophy occurs only in those forms of nephritis in which the glomeruli are diseased and in large part impermeable. He points out that in the forms of nephritis with degenerative epithelial lesions only, hypertension does not occur; it is peculiar to scarlatinal nephritis and contracted kidney.

This is an important field for investigation: first, as to tension in various forms of epithelial lesions, especially those of the acute infectious diseases; and, second, a cooperation between the clinician and the pathologist as to the relation of hypertension to histologic changes, with special regard to the glomeruli.

Experiments definitely demonstrate that the high pressure associated with glomerular lesions can not be explained by the earlier theory of diminution of vascular territory in the kidney. Loeb offers the following hypothesis:

Since the renal activity varies directly with the blood-supply, lesions of the glomeruli would limit local vasodilatation. When the renal activity demands more than the local conditions allow, the stimulus goes beyond the kidney and there is exerted reflexly a splanchnic contraction which leads to an increased systemic tension and then an increased flow of blood through the glomeruli.

This explanation, hypothetical as it is, brings out very prominently the fact that hypertension, be its cause what it may, is essentially a conservative process having for its object the maximum functioning power of the kidney.

Passler and Heineke have attempted to explain the problem by reducing the kidney substance of animals

by successive excisions. They found that after two-thirds to three-fourths of kidney was removed a certain proportion, about 25 per cent., of the animals developed a permanent increased tension with heart hypertrophy. In such animals it was also observed that arterial spasm with a further rise of pressure quickly followed certain stimuli which in normal animals would produce little effect.

They conclude that in the state of renal insufficiency so produced the heart hypertrophy is due to the increased work resulting from the tendency to arterial spasm and that this in turn is due to the effect of retained toxic substances.

So again we come back to the chemical theory of retention—all theories except that of vicarious adrenal secretion return to this point—but of the substances "retained" we know nothing. Herein is the problem of the "causes of hypertension in nephritis"—a problem to be solved only by the methods of chemistry and physiology directed by careful clinical observation.

P. C. Janeway (Prof. Soc. Exper. biol. and Med., 1909, vi, 108-109) has furnished a brief account of a study of the blood pressure in dogs with insufficient kidney substance. Instead of excising a portion of the kidneys he caused destruction by ligating some of the branches of the renal arteries. Also, instead of studying the pressure by direct measurements from the carotid, he modified the Riva-Rocci cuff so that the clinical method of taking blood pressure could be applied to the dog. Thus observation could be made from day to day with a limit of error of only 10 to 15 mm. Hg. I have found that a decided increase of blood pressure occurred after destruction of kidney substance by ligating. Thus in one animal, with an average pressure before operation of 90 mm., a rise to an average of 125 occurred after 100 days; and in another a rise from 117 to 150 mm. occurred after only 35 days. Janeway does not discuss the mechanism by which the hypertension develops.

NOTE.—I gratefully acknowledge my use of the literature of this subject as summarized by the following writers:

Müller, F.: Morbus Brightii. Verhandl. d. deutsch. path. Gesellsch., 1905, ix, 64.

Janeway, T. C.: The Clinical Study of Blood-Pressure. D. Appleton & Co., 1904, New York.

Pearce, R. M.: The Theory of Chemical Correlation as Applied to the Pathology of the Kidney. Arch. of Int. Med., August, 1908.

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THE VALUE AND LIMITATIONS OF SALT-FREE DIET AND RESTRICTION OF FLUID IN NEPHRITIS

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Whatever one says under this title must be said with some caution and with a right reserved to change opinion with advance in knowledge. Although nearly one hundred years have passed since the question of the nature of the toxic constituents of the urine was first submitted to experimental inquiry, it cannot be regarded as yet settled. We can not to-day name all the poisonous constituents of the urine. I am not going into the literature of this subject in this paper, because it is too voluminous, in many points contradictory in its findings and unsatisfactory in the conclusions reached. The following points seem to be fairly well established:

1. Urea and uric acid are not important constituents of the urine so far as their toxicity is concerned. I mean to say that neither of these can be regarded as the active agent in the causation of those symptoms that result from failure to function on the part of the kidney.

2. About 85 per cent. of the toxicity of the urine is due to its inorganic constituents, the most toxic of which is potassium chlorid.

3. There are present in normal urine certain organic poisons, the nature of which has not yet been ascertained.

4. Although the inorganic constituents, notably potassium chlorid, are markedly poisonous, they can not be regarded as standing in a direct causal relation to that

complex of symptoms which we designate as uremia. A small fraction of a grain of potassium chlorid, as I have frequently demonstrated, injected into a ventricle of the brain of an animal, may cause prompt death, but neither the symptoms nor the postmortem findings are those of uremia.

Of one thing I feel quite confident, and that is in withholding salts from our nephritics we are not withholding the direct cause of uremia. The best that we can hope for in the use of a salt-free diet is to protect the kidneys by decreasing to a certain extent their labor and thus conserving their capacity as organs of elimination. The inorganic salts, and certainly the chlorids of sodium and potassium, are not, singly or combined, the active and direct cause of uremia. Any inorganic salt above that needed in the processes of metabolism is without benefit to the body and increases unnecessarily the stress of work thrown on the kidneys, and, when these are already diseased, it is in accord with good sense to lighten their burdens so far as can be done without danger.

There are some reasons for suspecting that the inorganic salts of normal urine, carrying about 85 per cent. of the toxicity of this fluid, and the organic constituents, carrying the remaining 15 per cent. of toxicity, partly neutralize each other. At least it has been repeatedly found that the ash of urine is decidedly more toxic than the whole urine. This fact has been observed by Bouchard, Stadthagen and others. I have repeated this test several times with the urine of both herbivorous and carnivorous animals, also that of man, and have invariably found it true. It has been suggested that it is due to the conversion of the chlorid into a more poisonous carbonate on incineration, but I have been unable to find any evidence of carbonate in the ash which I have injected, and it has occurred to me that possibly there may be some neutralization between the inorganic and organic

constituents. This is a problem that seems worthy of more extended study.

There is evidence that an absolutely ash-free diet may soon disturb the health of a normal individual. Taylor[1] has prepared such food and used it himself. He says:

"The symptoms were those of lassitude until about the sixth day, when I noticed a great deal of cutaneous irritation and generalized muscular twitching with excitation of the reflexes. The equilibrium of the entire system became disturbed; I lost the power of sleep; the irritability was extreme. At this time the acetone complex appeared apparently suddenly. I therefore realized that I was near the danger point, stopped the experiment, resumed ordinary diet and within a few hours after the ingestion of alkalis, the symptoms disappeared entirely."

This experiment was repeated on two men by Goodall and Joslin,[2] who failed to induce the acidosis experienced by Taylor. This matter also needs further study. In all of these experiments the amount of sodium chlorid in the daily urine diminished to about 0.2 gm.

In dogs long-continued feeding of a salt-free diet materially reduces the acidity of the gastric juice. So far as I know, no experiments along this line have been made on man. It has been repeatedly shown, however, that it is difficult and probably impossible to reduce the amount of salt in the living tissues below a certain, fairly well-defined minimum. Life is no longer possible when this reduction passes this point. The molecules of living cells do not function when the content of inorganic salt falls below this minimum, which varies in different animals and in the different organs and tissues of the same animal. Notwithstanding all the excellent work that has been done on metabolism, we are hardly warranted in making more exact or positive statements on this subject. It is generally held that the chlorids of the urine are not in organic combination, but, as I have stated, it has been repeatedly found that the ash of urine

1. Taylor: Tr. Assn. Am. Phys., 1907, p. 245.
2. Goodall and Joslin: Tr. Assn. Am. Phys., 1908, p. 92.

is more toxic than the whole urine. Moreover, single inorganic salts may be more poisonous when injected intravenously than mixtures of several salts. There are, therefore, reasons for suspecting that the inorganic constituents of the urine are not only in part neutralized by the organic, but also in part by one another. The fallacies of Bouchard's method of determining the toxicity of the urine has been repeatedly pointed out, and his conclusions can not be accepted as final. Besides, it should be evident that poisoning due to the retention of normal constituents of the urine and uremia are two quite distinct and different things. Many years ago Rees reported a case in which there was only one kidney, and, this becoming blocked by a calculus, there resulted complete anuria. The man died, but not from uremia. Cases of prolonged suppression have been repeatedly observed and, although these may terminate fatally, death is not due to uremia. In uremia the poison results from a radical change in metabolism, and the active agent produced is not one of the normal constituents of the urine. It is possible that protein sensitization may give us more exact information concerning the nature of the poison elaborated in uremia. But the one point that I wish to emphasize in this paper is that poisoning from anuria and uremia are two distinct things, and, while the inorganic salts are the most poisonous constituents of the urine, their retention in the body can not be regarded as the cause of uremia—certainly not the direct cause.

In 1903 it was suggested by Widal that nephritic edema is due to chlorid retention, that with the disappearance of the edema the elimination of chlorid is increased, and that the proper treatment of the edema of nephritis should provide a diet that is largely salt-free. The reasoning in this statement seems to be good, but the experience of clinicians has not been so satisfactory as the earlier reports led us to expect. In Widal's first case the edema seemed to fluctuate directly with the amount of salt in the food and it was suggested that

the milk diet, so long and favorably known in the treatment of nephritis, might owe its success largely to the fact that it contains only a small amount of sodium chlorid. Moreover, there is some clinical evidence that edema does increase the danger of uremia. At least uremic symptoms have been seen to disappear with the disappearance of edema and to return with the accumulation of fluid in the tissue. That there is a causal relation between edema and uremia does not, however, seem probable, because the latter is frequently seen in interstitial nephritis when the former is absent or but slightly developed. Edema in nephritis is due to diverse causes, and certainly not always to salt retention. In acute nephritis it seems to be due to the effect of the poisons on the walls of the vessels. In many cases of chronic nephritis, edema is due to circulatory disturbances and is best combated by agents directed to these causes. In amyloid nephritis it is again toxic. In a certain small percentage of cases of chronic parenchymatous nephritis the edema is apparently markedly influenced by the quantity of salt in the food, and it is in these that the best results are obtained by reduction of the salt in the food. Even in these the improvement is limited to the reduction of the edema. I do not deny that this is of sufficient advantage to be worth doing. It seems to me that the greatest good is to be secured by restricting salt in the food of those patients who may be called prenephritics. We frequently meet with patients of this kind. They are men and women past the prime of life who have been unduly energetic, often of good habits, with the exception of the tendency to overwork. The heart has been unduly taxed; they get out of breath easily; occasionally they grow dizzy. Blood-pressure is high. There may be a trace of albumin in the urine or the most careful and frequent examination may fail to show this abnormality. I am in the habit of advising patients of this class to have their food prepared without the addition of salt. I do this for the following reasons: 1. They can educate

themselves to eat unsalted food. I am positive that we eat too much highly salted food. 2. With unsalted food they drink less. Vesicular fulness can be induced by water as well as by beer. 3. The kidneys are relieved of excessive work in eliminating excess of both salt and water. Otherwise I have never been satisfied that I have seen any benefit in any form of nephritis in denying the patient the satisfaction of his thirst.

Milk contains about 2 gm. of sodium chlorid per liter, and on an exclusive milk diet three liters per day supply the necessary calories for the average man. On such a diet the individual receives daily about 6 gm. of salt, and this seems to be all one needs in health or in disease. A mixed diet of unsalted meat, potatoes, bread, butter, fruit, sugar, cream or milk and coffee or tea of equal caloric value contains in the daily ration about 3 gm. of salt, and this may be increased by the addition of an equal amount if the taste is objectionable.

Time will not permit me to take up the interesting subject of the mechanism of nephritic edema, but I will call attention to a recent contribution to this subject by Bence,[3] who has shown that there is an increase in the volume of blood and edema appears in renal insufficiency even when there is no fluid taken into the alimentary canal; but, of course, both of these conditions are increased when much water is ingested. It seems only good sense, therefore, to limit the consumption of fluid in nephritis so far as possible without distress to the patient, but it should be understood that edema develops in experimental animals in which nephritis has been induced by the subcutaneous injection of uranium salts even when such animals are denied any fluid.

3. Bence: Ztschr. f. klin. Med., 1909, lxxvi, 69.

MANAGEMENT OF UREMIA

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For the purposes of this discussion, uremia may be tentatively defined as an autointoxication, which affects mainy the nervous system, and occurs in connection with renal insufficiency. It is due to the retention in the blood, tissue lymph and cells of the body of certain indeterminate, but specific, products of perverted, or normal, tissue metabolism, which are not excreted by the inadequate kidneys, or are not taken up by the lymphatic radicles, or are not neutralized or destroyed by the lymphatic glands or other protective organs.

We are lacking in knowledge regarding many of those fundamental facts of anatomy, physiology and pathology which are necessary for formulating a specific treatment for uremia; therefore, that which is offered should be considered as being based on a fairly rational empiricism, directed in the main toward the prevention and relief of prominent symptoms and known conditions.

In order that my remarks may not lack in directness and force by a discursive rambling over too broad a field I shall confine myself to a consideration of some of the problems in the management of uremia, with particular reference to the disturbances of the intravascular and extravascular circulation, in that protean malady technically known as chronic interstitial nephritis, as they have been encountered in my personal experience.

Fairness impels me to say that the exigencies of this occasion renders it impossible to give consideration to

the many interesting features connected with the treatment of such strikingly important symptoms as convulsions, coma, Cheyne-Stokes respiration, mental aberration, etc.

On making a diagnosis of chronic interstitial nephritis the physician should make earnest efforts toward preventing the development or recurrence of recognizable uremia. The patient should be informed of the nature of the disease, and given a tactful prognosis and directions for its management as to diet and general regimen. The diet should be individualized and specifically prescribed; it should be so arranged, along the ordinary established lines, as to maintain nutritive equilibrium at the highest possible level, with the smallest total amount of proteid and carbohydrate foods. The total liquids should be so adjusted as to carry off the largest amount of excrementitious materials, as may be determined from time to time. The regimen should consider such important matters as residence, clothing, occupation, exercises, environment, etc. The amount and character of the physical exercises must be adjusted to meet varying capacity and requirements. Extraordinary care should be taken to avoid infectious diseases. The patient should be seen with such frequency as to allow the physician to keep closely in touch with his ailments. At these times modern methods of examination should be the rule. The patient should consult his physician promptly on the advent of any one of a series of significant symptoms, a list of which he should have. The physician should be intelligent, alert, assiduous and tactful; in every legitimate manner he should endeavor to obtain and retain the confidence of his patient, solely because it is to the latter's best interests.

Mention is frequently made of the sudden and unexpected onset of uremic manifestations; but we may well inquire whether this is often really without warning. Looking back over my experience, I recall several instances in which an uremic attack was ushered in with

a celerity which was, at the time, truly surprising; yet when these cases are reviewed in retrospect none was without ample symptomatic warning. Certain it is that when excessively high blood-pressure, various dyspneas, edema, transient blindness, retinitis and retinal detachments, dizziness, headaches, neurites, drowsiness, impairment of the sense of location, mental perversions, tremor and cramps, aphasia and fleeting paralyses, cardiac enlargement and insufficiency, vomiting and diarrhea, cutaneous affections, etc., thrust themselves, singly or in groups, obtrusively before us, we should appreciate their diagnostic significance.

As is well known, the blood-pressure is abnormally high in these cases. Perhaps the dietetic and other measures instituted may limit, or possibly prevent, further advances along this line. Rarely, as time passes, the vasomotor nerves so accommodate themselves to the unknown irritant that the circulatory balance is adjusted in such manner that the blood-pressure remains stationary, or even declines somewhat; and this without notable cardiovascular failure. The exalted cardiovascular tension may be somewhat reduced by various medicaments, as, e. g., hippurate of ammonia, lichenin, the nitrites, the iodids, thyroid extract, etc. The clinician must decide whether any measures should be taken to bring about this result; and, if so, under what circumstances, and by what means. Ordinarily the high tension is conservative and should not be interfered with. In some instances, however, there occurs a rapid rise of pressure above the patient's usual high level, with increase of the hazards accompanying this abnormal state. These sudden exaltations of tension are often followed by failure of the delicately balanced cardiovascular-areolar tissue supporting tension. Under these circumstances, with the patient in great distress, rupture of degenerate vessels threatening, and a practical certainty that circulatory incompetency will soon occur, I am of the opinion that

the patient's best interests are served by anticipating the near-inevitable by artificially lowering the excessive pressure—if this can be effected. If the condition is urgent a free blood-letting should be done; otherwise one of the slower methods may be chosen. In this manner the patient is given the greatest relief, and imminent danger averted; but the underlying conditions remain, and the physician should not be lulled into a sense of security, as the patient is likely to be, by the ease and comfort which is now his. Experience proves that, once lost, the complicated circulatory balance is seldom fully and permanently restored. Not infrequently circulatory insufficiency follows an acute infection, or other depressing influences, without the patient experiencing the extreme tension referred to. In such cases the hypertrophied heart dilates, valvular incompetence may be added and the well-known results of cardiac failure appear, possibly to an overshadowing degree. In this connection especial consideration should be accorded to the overfilling of the lymph spaces, and the subsequent failure of the areolar tissue-lymph tension, with edema as the final result.

The rôle of edema in the genesis of uremia is most important, although it will be practicable, in this paper, to note only some of the most significant features. Thus, in many cases, without gross evidences of edema, the intercellular and areolar tissue spaces become distended with lymph to a degree which induces a high tension. The patient is plump; the soft parts are resistant to pressure, but without pitting; the integrity of the areolar tissues as a series of restraining membranes is maintained; anasarca is not present, but is imminent; the condition might be termed occult edema. Under these circumstances the lymph circulation is impeded, and toxic waste products and specific toxins begin to accumulate, with uremia probably in its incipiency. Edema in chronic interstitial nephritis is usually of the incipient or occult variety, and infrequently does it be-

come obtrusive; general anasarca is rare in uncomplicated cases; when dropsy becomes a prominent feature it is due to cardiac incompetency, and partakes of the general character of cardiac dropsies, with one important and fundamental exception, i. e., that the patient is more or less uremic. The bearing of this distinction on our conception of the essential nature of uremia should be given full weight. Thus it follows, logically, that, inasmuch as the physical conditions are alike, the uremia of the cardionephritic dropsical patient is due to vital, and not to mere mechanical disturbances. It is significant that, in my limited experience, the serum obtained from the liquid bowel movements of such nephritic patients has been much more heavily laden with chlorids, and often with sulphates also, than in others with pure cardiac dropsies.

Edema interferes greatly with the composition of the blood and the extravascular lymph, and with cellular nutrition. The capillaries and lymphatic radicles are compressed, with interference with their functions; the tissue lymph becomes stagnant and laden with specific toxins and tissue-waste materials; the extravascular circulation is short-circuited. There is an extraordinary lack of easily obtainable information concerning the physiology and pathology of the circulation of the tissue lymph. For our purposes let it be assumed that the nutritive elements of the blood, proteid and other, in aqueous solution, are transfused through the capillary walls by selective vital cellular action, assisted by simpler mechanical forces; that the extravascular lymph, carrying both nutritive and waste materials, circulates, vitally and mechanically, in the intercellular channels and areolar tissue storage spaces, and by a selective excretory function of the cells of the lymphatic radicles, finds its way into the ducts and thence through the glandular protective filters into the blood current.

In my opinion, special consideration should be accorded the management of every degree of edema—

occult as well as manifest—in nephritics. As the result of long-continued and fairly broad observation I commend the following plan of treatment, modified to meet varying and individual conditions:

During the first day the diet should consist of thin gruels, cream and water, vegetable soups, tea, coffee, cocoa, water and carbonated waters. From these there should be omitted the gruels on the second, and soups on the third day; during the fourth and fifth days very little should be taken; on the sixth day the soups should be replaced, and on the seventh day the gruels; later the ordinary careful dietary of the nephritic should be gradually resumed. Every night of the first three days the patient takes 10 grains of mercurial mass, in two recently made pills of 5 grains each, followed by an efficient sodium or magnesium saline in the morning. Beginning on the fourth morning, after free action of the saline, there is given 1/30 grain pure elaterin hourly for three doses; 1/24 grain every two hours for three doses; finally 1/18 grain every three hours until ten or twelve copious watery bowel movements have been induced. During the last series of doses the intervals may well be p. r. n., or as specially directed. Subsequent to the discontinuance of the medicine there will be several more of the liquid evacuations. The elaterin must be pure, and it is preferably given in powder, with sugar of milk and finely powdered ammoniated glycyrrhizin. During the time the elaterin is being given the patient should remain in bed, using the pan. He should be informed of the abdominal distress, nausea and vomiting which the drug sometimes induces. Without giving reasons for the opinion I am quite sure that, if satisfactory results are to be secured, it will be well to follow closely the spirit of these suggestions in regard to diet, medicine and general regimen as detailed.

The treatment here recommended will usually drain from the bowels a considerable amount of serum, varying in total volume from 4 to 15, or more, pints. The

serum is usually acid; straw-colored; of from 1005 to 1030 specific gravity; free from albumin; laden with urea to 0.01 per cent. to 0.2 per cent, phosphates to small percentage, chlorids to 3 per cent. to 25 per cent. and sulphates to 1 per cent. to 10 per cent., by volume. The odor is sometimes peculiarly offensive. There is no doubt, in my mind, as to the fact that the serum passes into the intestine by secretory action.

During the period of alvine drain renal activity is reduced; subsequently the flow of urine usually becomes very free, often continuing so for many days, even until the cardiovascular-sanguineous and lymphatic-tissue lymph balance of the circulation has been restored. In the most successful cases the urine is not only increased in quantity, but in urea content as well—rising in one instance to the enormous output of 994 grains during a single twenty-four-hour period. In some unsatisfactory cases—rare in my experience—the flow of urine is not augmented; the overstretched areolar tissues fail to regain their resiliency; the current of tissue lymph toward the lymphatics is not maintained—possibly it had not been attained; edema continues or increases.

This initial part of the treatment, in typically successful cases, is followed by subsidence of the objective and subjective symptoms—uremic as well as circulatory—with such relief to the patient that it may be fairly described as profound. Much of the improvement appears promptly; more is noticeable during the following two weeks; the full measure of benefit, however, is not obtained until about the end of six weeks, and a surprising proportion during the last few days of this period. The improvement usually continues for several months; it may be of short duration; occasionally the period is remarkably extended.

In whatever manner the relief may have been induced it is probable that it may be made more complete and greatly prolonged by close medical supervision and persistently careful management. For this reason I have, for

many years, advised these patients to take daily systematic, well-considered and individualized, active exercises of such character as to bring into play as many as possible of the muscles of the body. Whenever necessary this is supplemented by general and vigorous massage. The object of these measures is to facilitate, forcibly, cellular activity. The results have been so satisfactory that I commend these methods for consideration.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. CHRISTIAN, MUSSER, VAUGHAN AND WELLS

DR. D. L. EDSALL, Philadelphia: It is very clear that a great many erroneous conclusions have been reached in the vast amount of literature that has accumulated on this question. There is no constant relation between the retention of chlorids and edema and the severity of the nephritis. There are, then, various reasons why the theories concerning the extremely intimate relation between edema and the chlorid disturbances are not established. There are also errors in regard to the conception of the cause of alterations in chlorid excretion, for reduction may, on the one hand, clearly be due to a reduction of the capacity of the kidneys to excrete chlorids, while in some instances it is certainly due to alterations in processes going on elsewhere than in the kidneys; and at times the latter are probably definitely conservative processes, designed to relieve the kidney of its work of excretion, and the edema itself becomes a conservative process, partly to relieve the kidneys and often largely to relieve the circulation. A reduction in the amount of sodium chlorid ingested, aside from any influence on edema, helps largely to reduce the work that the kidneys do.

I saw this fact strikingly illustrated some years ago in some experimental observations I made in regard to the possible value of studying the excretion of definite doses of sodium chlorid as a means of testing the functional capacity of the kidneys. I gave sodium chlorid to various persons who appeared to have about the same degree of damage of the kidneys, some of them having actual nephritis and some of them simply arteriosclerotic changes. I several times met with observations which made me give up the studies because it was clear that there was danger attached to such a test; that is to say, I found in several instances that an amount of sodium chlorid no more than equal to what is taken in an ordinary diet, produced evident and sometimes marked increase in the incapacity of the kidneys to carry out not only the excretion of sodium chlorid, but excretion in gen-

eral, of water as well as of the solids, was largely cut down. It is clear then that an amount of sodium chlorid not more than equal to what is contained in an ordinary daily diet may cause decided failure of function on the part of the kidney even in cases in which the kidney appears to be doing fairly good work. Hence, whatever we may think concerning the theories of the relation of salt to the symptoms of nephritis it is certainly a valuable procedure to limit the amount of table salt in the diet. This same point has been elicited in another way recently in some work that Dr. Lavenson has been doing in my laboratory in regard to the influence of certain potassium salts on the excretion of chlorids in the urine, basing this work on the statement of Bunge, which has not been generally accepted, however, that potassium salts cause a decided increase in the excretion of chlorids. There seems to be little doubt that Bunge is right about this, for Dr. Lavenson found a decided increase in chlorids after a variety of potassium salts. The nitrate which has been considered to have an especial action did not appear to be particularly active as compared to the others, the effect exerted being apparently in direct relation simply to the amount of potassium given. Dr. Lavenson naturally tested the suggestion that at once comes from this that potassium salts might be a good method of overcoming chlorid retention. The result proved to be merely an instance of the fact that when we attempt to do what superficially appears to be right, we may do harm. The retention of chlorids appeared to be in some cases definitely a protective thing, and urging the kidneys to excrete more chlorids simply did harm, the general excretion being reduced, although the chlorids might increase or decrease—actual toxic symptoms developing in one case in mild form. There is one more point that I would lay stress on: That is, we should approach all these conditions with the idea that they are largely dependent on intoxication and the best way to relieve intoxication is to start by relieving the amount of work demanded of the eliminative organs as far as we can. Satisfactory results can sometimes be obtained in these cases by placing the patients on actual starvation for a brief period, sometimes a day and sometimes several days. This gives an opportunity for improvement in the digestion and the metabolic and excretory functions through giving them a partial rest. It is of course necessary when carrying on starvation for this or any other purpose to be very watchful of the effects, as it is a serious procedure, but in these cases it is necessary to undertake serious measures, and the reduction of the diet to nothing but water or to say a pint of skim milk in a day, to which water is added, will sometimes accomplish very comforting results, which are not obtained when an ordinary full milk diet is used.

DR. DELANCEY ROCHESTER, Buffalo, N. Y.: There are two practical points I should like to speak about. First, it strikes

me that salt-free diet is valuable in those cases in which there is much edema, because of the fact that in the fluid and in the tissues of the body there is a considerable amount of sodium chlorid which will supply its needs. Dr. Vaughan has shown that the tissues of the body need chlorids to a considerable extent; if we withhold them from the food, Nature has provided a source of supply in the serum of the edematous fluid, which may be called on when they are in demand. I should think that if the fluid ingested be restricted, fluids could be obtained from this same source. Second, in the management of uremic attacks I wish to commend Dr. Wells' procedure, but in addition, there is one thing used in these cases which I find of special value—the action of the skin as an eliminative organ. I have found it very useful to administer, ten or fifteen minutes before giving the hot water bath or hot pack, minute doses of pilocarpin, 2 or 3 mg., it aids greatly in producing profuse sweating in these patients. Elaterium has also been recommended. I have used it in smaller doses and continuously—perhaps 8 mg. twice a day. It does not produce nausea, but drains the bowels and is of great advantage in these cases.

Dr. James Tyson, Philadelphia: Dr. Christian's paper was one which has so thoroughly covered the lines with which I am practically familiar that I hesitate to say anything on the subject or on what he has brought out. I was struck, however, with the apparent differences of result in experimental nephritis as compared with the symptoms that are observed clinically. I was also impressed by what was said as to the sorts of casts which first make their appearance in producing experimental nephritis. In actual experience the cast that appears first is usually the hyaline cast, and not the granular cast. This is seen in the passive congestion due to cardiac disease which permits a leakage. As the seriousness of the condition grows the granular cast appears, becoming more and more granular, *pari passu*, with the destruction of the cells. What Dr. Christian has quoted as experimental facts are probably correct, but they do not agree with my experiences in the study of the urine in actual cases. With regard to the treatment of high tension, Dr. Musser has struck the keynote, but not enough stress was laid on the impropriety of treating high tension *per se*. To strike at the root of the evil, one must remove the cause of the high tension. In this respect, Dr. Edsall's statements on the matter of starvation are sustained by my experience. Many years ago I taught the treatment of nephritis by small quantities of milk, or as little food as possible. This was not for the purpose of relieving the uremic symptoms any more than to remove the edema and the vascular symptoms of an unfavorable kind.

Dr. John A. Lichty, Pittsburg, Pa.: When a slight cerebral hemorrhage occurs in these cases, the blood-pressure immed-

iately drops and remains down a longer time than one would expect it to do when rest is ordered. There is no trouble at all in keeping the blood-pressure, which was 265, down at 195 or 210, while the patient is leading a rather active life. These patients are of course thoroughly frightened and are willing to follow a regimen now of rest, diet, etc. But the drop in the blood-pressure is very sudden and will remain lower for a longer time than one would expect.

I should like to refer to two patients with chronic appendicitis whom I have had operated on during the past year in which there was a history of nephritis of some years' standing; I of course had to consider the safety of an anesthetic. Ether narcosis produced absolutely no disturbance of the urinary secretion. The first patient was 24 years old and had had scarlet fever when 3 years old, and was afterward sent to Dr. Tyson of Philadelphia and Dr. Janeway of New York, because of the existing nephritis. Albumin and casts remained in the urine year after year. It was decided that an interval operation for appendicitis should be done. Very great care was taken in giving the ether, and there followed no disturbances in the urinary secretion at all. The second patient, twelve years ago, had had diphtheria and a general anasarca afterward. Dr. Osler saw this patient and pronounced the condition a very severe case of parenchymatous nephritis. This patient also had to be operated on for appendicitis. The ether narcosis had no evil effect on the kidney secretions.

A third patient, however, with no signs of nephritis, did quite differently. This patient had normal urine, and was operated on under ether narcosis. After the operation there appeared an acidosis, casts, albumin, etc., and death due to anuria occurred within twenty-four or thirty-six hours after the operation. With such diverse experiences it seems to me that after all our knowledge of this condition, so far as it applies to the individual patient, is not of very great practical value.

Dr. John N. Upshur, Richmond, Va.: I want to protest against the administration of morphin or any opiate as a temporary palliative in the treatment of uremia;; it certainly does interfere with secretion. The thing we should do in cases of grave uremia is to direct our work as much as possible along lines of safety; therefore, if we can give rest to the kidneys and at the same time get elimination we can accomplish much more and do much better than if we get our head in the bushes like the ostrich, by giving morphin, and think we are accomplishing something.

If we can give rest to the kidneys by placing the patient in a hot pack and by hydragogues cause elimination through the bowels, we will find that we not only give relief from the grave uremic symptoms, but through the elimination through the skin and bowels at the same time we can reduce the amount of tension in the blood vessels. The error we are

liable to fall into in patients who may and do have renal trouble, is that we do not make sufficient analyses of the urine and do not get the careful knowledge of what is going on by such a systematic urinary analysis. We are all apt to err in this direction. Even in those cases in which there is no suspicion of renal lesions we should keep in touch with the condition of the kidneys by a careful observation through urinary analyses; this should be made a routine matter.

DR. WALTER L. BIERRING, Iowa City: It seems to me that sufficient emphasis has not been given in this discussion to the special reference made by the last speaker in the symposium on the relation of circulatory disturbances to uremia. Whatever conception we may have as to the nature of uremia I am sure we recognize that the appearance of its symptoms is largely dependent on the maintenance of the cardiovascular balance, and the real problem of treatment at the present time is to anticipate and control, so far as possible, the cardiovascular disturbances.

DR. HEINRICH STERN, New York: Dr. Christian mentioned in parenthesis that the excretion of albumin via the kidneys can only ensue on the basis of a diseased condition of the latter. Evidently he has not consulted some of the latest literature on this subject. Langstein, in his thesis *"Die Albuminurien älterer Kinder,"* which appeared in 1907, stated that there may be albuminuria without a corresponding renal lesion. Langstein was the first to perform an autopsy on the body of a patient who had been affected with authenticated orthotic albuminuria. This patient, a girl of 10, was under his observation from March, 1903, until November, 1905, and although considerable amounts of urine were excreted, the urine never exhibited any renal morphologic elements. Autopsy revealed nothing abnormal in the kidneys, and careful microscopic examination demonstrated entire absence of degenerative or inflammatory changes. Ottmar Rosenbach, who died a year or two ago, said long ago that there may be a regulatory albuminuria occurring independently of a structural affection of the kidney. Rosenbach has shown that it is the condition of the blood, the inability of the latter to attach to itself all the albumin which has found its way into the blood current, to which is due the excretion of the large albumin molecule through the kidneys.

It is not a diseased kidney which permits the transudation of the albumin, but a strong and healthy kidney. I should say that the healthy kidney is always permeable for the albumin molecule, but that the blood which attaches itself to the albumin and then deposits it in the tissues whence it is again taken up by the return circulation in the form of urea, does not permit the escape of the blood proteids prior to their intrasystemic disintegration. While, therefore, albuminuria is a pathologic occurrence, its causative factors are not situated in the kidneys but are distinctly anterenal.

Although Dr. Wells has not brought out anything substantially new, he has developed some new view-points and interpretations. I know that he has not especially entered into a clinical subdivision of the uremic states. I think, however, that it is impossible to apply rational treatment unless one knows the basis on which the uremia has developed. For instance, in the large white kidney, the passage of urine is seriously interfered with; in contracted kidney, on the other hand, there is nothing to prevent its excretion. The sera of uremia on the basis of chronic parenchymatous nephritis are differently constituted in some major points from those of uremia due to interstitial nephritis. In parenchymatous nephritis there is a tendency to convulsive phenomena, in interstitial nephritis to a comatose state. This important divergency is explained by the different constitution and physico electric behavior of the respective sera. I have shown that there is no chemico-toxicity which stands at the foundation of the uremic phenomenon, that there is not a single substance, known to us, excreted by the urine or the other excrements, which is apt to bring about either the convulsive or the comatose phenomena. By retention nitrogen in the blood is understood all the nitrogen remaining in the liquid after complete removal of the albuminous substances. The average amount of retention nitrogen in 100 c.c. of normal blood serum is between 25 and 30 mgs.; in chronic parenchymatous nephritis without uremia the average amount is 40 mgs. and in the presence of uremia about 62 mgs. in 100 c.c. blood serum; in chronic interstitial nephritis without uremia an average amount of 82 mgs., and when uremia prevails 130 mgs. retention nitrogen were found. These figures show that in the blood serum of chronic parenchymatous nephritis about 35 per cent. more retention nitrogen is contained than in the normal liquid; that in interstitial nephritis the retention nitrogen is present in twice the quantity as in the parenchymatous variety, and that the retention nitrogen is augmented in the uremic states consequential to the nephritic conditions. The enormous amounts of retention nitrogen in the serum of chronic interstitial nephritis undoubtedly stands in causative connection with the natural termination of the disease-uremia. In parenchymatous nephritis uremia is not only a much rarer but also a less grave complication. This I have explained by the fact of the relatively small amount of retention nitrogen. The inconsistency of pursuing the same plan of treatment throughout in the various cases of uremia which are so unlike in their manifestations and have risen from such distinctly discrepant substrata is obvious. I think it is unwise to speak of the management of uremia, when this uremia may mean that we may have at least two entirely different states to deal with. One cannot be treated like the other.

Some one said that morphin was contraindicated in uremia. This has to be taken with a grain of salt. In the uremia of chronic interstitial nephritis, which is characterized in almost every instance by a condition of tranquil coma, very rarely exhibiting convulsive phenomena, morphin is certainly contraindicated, because it also causes coma and may thus aggravate the existing comatose condition and hasten a fatal issue. On the other hand, in the uremia of chronic parenchymatous nephritis, which is characterized by convulsive seizures, morphin may have a distinct value when chloroform has proved of no avail. Its efficacy in controlling the convulsions may be due to the retardation of the metabolic processes ensuing from its administration, thereby preventing further accumulation in the blood of catabolic substances, and to its augmentation of vascular tonicity.

DR. BOARDMAN REED, Los Angeles, Cal.: I wish to confirm the observations of Dr. Tyson of Philadelphia and Dr. Smith of Baltimore regarding the value of therapeutic fasting or starvation, not only in fevers but in other conditions. We know that in gastric ulcer and, in my experience, in hyperchlorhydria, the good results which follow starvation for a few days when the patients are put on a light diet, particularly in patients with high tension. In treating patients with arteriosclerosis and hypertension splendid results follow placing them on a low diet, or even actual fasting for three, four or five days. In cases of high tension it is perfectly safe, particularly if the pulse be watched carefully to see that the tension does not get too low. Only recently we have come to appreciate what can be done by fasting for a few days, and particularly its influence on conditions in the gastrointestinal tract. It seems to be the only way so far discovered of getting rid of the bacterial cause of the trouble in certain cases.

DR. HUGO A. FREUND, Detroit: I find that too little mention has been made of the value of observing hypertension systematically. This one thing as suggested by Dr. Bierring should be carefully watched in each case we are treating. It is very essential to note the condition of the cardiovascular system in connection with the urinary findings. I do not believe, however, in the desultory examination of the blood-pressure with the sphygmomanometer, taking the blood-pressure one morning, then the next, and so on, but I do urge its systematic use. A competent nurse or assistant can be trained to take two-hourly readings. These, when charted, give us most valuable curves that aid in the immediate treatment and in the prevention of otherwise unavoidable accidents. In many cases an oncoming uremia is shown a long time before the patient is seized with convulsions or other disturbances make their appearance.

DR. CHARLES F. HOOVER, Cleveland: It has not been clearly stated whether we are dealing with a cardiovascular problem or an impairment in renal elimination or uremia. There seems to be a lack of clearness on the part of the speakers as to what phase of nephritis these therapeutic efforts have been directed.

DR. HENRY A. CHRISTIAN, Boston: In the paper I simply discussed the acute toxic nephritides. If an animal be given a small dose of these irritating substances and then examine the urine you will throughout the course of the observation find in the urine simple hyaline casts. It does not follow that those casts have been hyaline from the beginning of formation. It simply indicates that a considerable time has elapsed between what has been formed in the kidney and what appears in the urine. If certain cases of cardiovascular disease be observed, we all know that only hyaline casts will appear during the time of observation of this condition unless there is an acute exacerbation when the granular casts appear. Apparently from experimental work the following explanation will serve for these cases. The casts are formed in small quantities, and the formation takes place slowly because the irritant used is small in amount, or the irritant present in the human body is small in amount. The casts do not make their appearance in the urine for a considerable period of time. In the time elapsing between their formation in the kidney and their appearance in the urine they have become homogeneous and consequently hyaline. This condition can be repeated with ease in animals. There is no discrepancy between the clinical and the experimental findings. Two factors must be considered, the time relation of cast formation, and the time relation of cast excretion. It is the period between these two occurrences that determines whether the casts will be hyaline or granular. At the same time it must be acknowledged that there is always a chance for error in arguing from animal experimentation directly to man. So far as we are able to judge, the method of formation of casts in animals is probably the same as in man; but of this, however, we are not certain. It was my intention in the paper to adhere to the consideration of the title, "Experimental Nephritis," and no mention was made of various other types of edema and renal lesions because this was considered beyond the scope of the paper. Albuminuria without renal lesion, as referred to by Dr. Stern, has so far as I know, never been produced in animals, and anyhow is hardly a part of a symposium on nephritis.

DR. JOHN H. MUSSER, Philadelphia: We must remember that hypertension is a curative process; therefore, any attempts to remove it entirely, especially after degenerative lesions secondary to the process have arisen following the

intoxication, will be and should be in vain. What we must do is to reduce such hypertension to the normal for that individual. I have made the same observations as has Dr. Lichty in regard to the fall in the blood-pressure and the persistence of that fall after an attack of apoplexy. In subsequent attacks the fall is very great, and it is probably due to the attack. Afterward the blood-pressure does not rise to the same point. In considering the treatment, I did not refer to the dietetic management so strongly as I should, especially in regard to the limitation of the amount of food taken and the proper selection of food. One must rely on the results of a study of the function of the stomach in determining the line of diet, plus the general broad principle of the limitation of the amount given. I want to refer to the use of two drugs. First, iron which is administered not only for the hypertension but for the degenerative lesions that accompany it. This remedy is of the greatest value. It is not only, it appears to me, a drug which supplies iron to the blood, but it also has some nutritional effect on the cellular structures. Undoubtedly iron does, as observed years ago, lower the blood-pressure when its use is prolonged. In cases of myocardial disease, and indeed I might say in cases of cardiac disease with dilatation, if I had to decide in an emergency of acute dilatation what remedy to use, I would prefer iron to digitalis. This agent, however, should be kept up for a long period of time. I should like to refer to opium as a remedy of great importance for the neurosis which attends this condition, either as a factor secondary to the intoxication or secondary to the hypertension. Small doses of opium or morphin give most satisfactory results in securing that equanimity which is so necessary; it aids in keeping down the stress and strain incident to the increased blood-pressure. Finally a word in regard to the use of mineral waters or the purgatives we select. Unless we are very circumspect in this matter we will find patients taking purgatives containing too much sodium chlorid and bring about renal inhibition. I recently saw a case in which a large amount of saline purgative was used when it was not indicated; the result was a progressive increase at that time of renal insufficiency and consequently dropsy. Stopping the salt was sufficient to bring about the renal activity and a subsequent lessening of the amount of dropsy.

DR. EDWARD F. WELLS, Chicago: It should have been noted that I limited my paper to the discussion of certain clearly outlined conditions, i. e., uremia as it appears in chronic interstitial nephritis, with special reference to the lack of balance of the circulation and especially the extravascular circulation and the tissue lymph. This was done for the reason that in the fifteen minutes at my disposal it was

impossible to go into all the different varieties of uremia, and the prevention of its causes. In my paper I laid particular stress on one point, or one sentiment, namely: the patient should be nourished to the highest attainable level with the least possible amount of food; and this applies with particular force to the proteids and carbohydrates ingested. It is astonishing to those who have not given much attention to the matter how comparatively little food is required for this purpose. Patients can be nourished on two-thirds, one-half or even one-third of what they are accustomed to take and maintain their weight, retain their vigor and increase their sense of well-being; this I have demonstrated in several instances. The trend of my remarks is this: The oncoming of uremia is manifested clearly by shadows cast before. One of the most significant of these foreshadowings is an endemic state, or usually an occult edema, in which the intracellular spaces are distended with fluid, and to a high tension. Such patients may be deprived of the excess of extravascular liquid with the loss of from five to twenty, or more, pounds in weight in a few days. Certainly this total loss in weight is due wholly to the loss of liquid and not to that of fat or the solid tissues of the body. In the cases in which the edema is occult, more or less manifest, I believe this to be an extremely important matter. The extravascular fluids contain an abnormal amount of certain salts, markedly differing from the proportions ordinarily contained in the lymph; therefore, the extravascular circulation is either overlooked as a whole, or portions are short-circuited. This is demonstrable in anasarca in which the legs are edematous; if indigocarmin be injected in the leg, it may be a very long time before it appears in the urine, and hours before it is noticeable in the serum of the opposite leg, or the serum may be drained from the opposite leg without getting a trace of indigocarmin. It has been short-circuited. It is to this condition that I wished particularly to call attention, not only because of its importance, but because I believe that it is either not sufficiently recognized, or due attention has not been given to it. The method of drawing off the liquid through the intestines is one of the many measures for the reduction of the edema which may be adopted; but on the method employed will depend its success or failure. If one gives elaterium he is sure to be uniformly dissatisfied with the results, but if he will follow the lines suggested definite results will be attained. With regard to occasional starvation, this, too, is a method which can be used, and is an essential feature of the method advised in the use of elaterium. The patient is practically starved; but he can live a long time without the ordinary foods. However, one may drive the nutritive portions of the blood out into the intracellular and lymph spaces; but stimulating the cellular secretory action in order to induce a return

flow of the waste-laden and toxic lymph back into the general vascular circulation is not such a simple procedure. The serum obtained through the intestines by the use of elaterium is in the nature of a vicarious elimination, which is brought about by secretory action and not solely as the result of pressure. The fluid may be readily obtained clear by filtering, and is free of albumin; there may be a mere trace of it perhaps, but when such is the case it is accidental and due to the open spaces left by broken-down epithelium. The tissue lymph is albuminous and contains salts in a different proportion than is found in the serum drained off through the intestines.

DIET IN TYPHOID FEVER

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The conclusions which I have reached concerning the food requirements of the typhoid fever patient are based on studies on the protein metabolism of the disease which have been carried out in Bellevue Hospital and the Department of Experimental Pathology of Cornell University, in collaboration with Dr. P. A. Shaffer, during the last two years.

I believe that the solution of the essential problems of the typhoid-fever diet will be found in the correct answers to two questions:

I. Shall the typhoid fever patient be given enough food to meet his energy requirements?

II. How much food may be considered necessary to fulfill these requirements?

It is obvious that the digestibility and general suitability of the various foods can not be ignored, and these will be referred to later.

I. SHALL THE TYPHOID FEVER PATIENT BE GIVEN ENOUGH FOOD TO MEET HIS ENERGY REQUIREMENTS?

Brief reference to the history of typhoid diets will assist us in finding the answer to this question.

Starvation was the accepted practice for centuries in fevers of all kinds, and included deprivation of water. Graves[1] (1835) convinced himself that, for want of

1. Clinical Medicine, New Sydenham Society, 1884, I, 136.

food, the ill effects of starvation were added to the ravages of the disease and recommended a diet which at that time was considered revolutionary. The diet consisted of carbohydrate-water made from toast-crumbs, meat-broths and jellies. It is difficult to estimate the caloric value of Graves' diet, since exact quantities are not mentioned, but at the most liberal reckoning it furnished not more than 300 calories in 24 hours—the equivalent of about 10 ounces of milk. Graves' belief that patients were benefited by this meager diet was shared by the great Trousseau and other eminent men of his time. The next advance in the feeding of typhoid patients was due, according to Nichols,[2] to the teaching of the late Austin Flint. Flint popularized the milk diet (about 1870). The usual quantity of milk taken by a typhoid patient in 24 hours—2 quarts—furnishes about 1,400 calories. The milk diet remained unchallenged until 1892, when Peabody's[3] paper, questioning its suitability, was published. Since 1892 there has grown up a school of practitioners who advocate liberal diets. Among them may be mentioned Shattuck,[4] Barrs,[5] Bushuyev,[6] Fitz,[7] Mueller,[8] Manges,[9] Kinnicutt[10] and LeFevre.[11] Bushuyev is the only one of these authors who has mentioned the quantities of the various foods to be given, and, therefore, the caloric values of these diets are difficult to estimate. Bushuyev's diet furnishes approximately 2,000 calories a day.

Thus, in each of these three diet-periods, there has been an increase in the energy value of the food recommended—an increase of 1,100 calories a day from Graves to Flint and a further increase of 600 calories

2. Diet in Typhoid Fever, Fiske Fund Prize Dissertation, Providence, 1907.
3. Diet in Typhoid Fever, Med. Rec., 1892, xlii, 620.
4. THE JOURNAL A. M. A., 1897, xxix, 51.
5. Brit. Med. Jour., 1897, i, 125.
6. Progressive Med., 1899, i, 328.
7. Boston Med. and Surg. Jour., 1899, cxli, 509, 526.
8. Therap. d. Gegenw., 1904, vi, 23.
9. Med. Rec., 1900, lvii, 1.
10. Boston Med. and Surg. Jour., 1906, clv, 1.
11. Med. News, 1904, lxxxiv, 11.

from Flint to Bushuyev. With each addition to the diet the statement has been made that the patients have been benefited. With respect to each addition, the profession as a whole has been perhaps too conservative.

Since the chief objections which have been raised to the liberal diets relate rather to the physical state of the food than to the amount of energy they furnish, no attempt will be made at this time to answer them.

The history of diets in typhoid fever, then, clearly indicates a steady, but very slow, tendency to increase the amount of food allowed to the patients. Only exceptionally to-day do we find physicians, once they have used the higher caloric diets, advocating a return to the older methods, and as a rule their arguments are based on questions of digestibility rather than on the energy value of the foods. McCrae[12] has expressed the opinion that more harm may result from overfeeding than from underfeeding, but he is evidently referring to the possibility of setting up digestive disturbances. A distinction must be made between properly nourishing and improperly feeding a patient.

Turning from the history of the typhoid diets and the claims which have been made for them, we may inquire whether there is evidence that definite harm may come to a patient through partial starvation. It is well known that partial starvation lowers the resisting power of healthy persons, and there is reason to believe that immunity to infective diseases is not so readily acquired when patients are undernourished. Healthy laboratory animals develop a better immune serum than those which are not robust. Ewing[13] believes that many of the clinical and pathologic phenomena in severe cases of typhoid fever are directly attributable to an autointoxication resulting from the excessive destruction of body tissues. Furthermore, Ewing and Wolf[14] state, in

12. Modern Med., 1907, article on "Typhoid Fever," p. 211.
13. Proc. Path. Soc., Philadelphia, 1905.
14. To appear in Arch. Int. Med.

a recent study of the urinary nitrogen in typhoid fever, that "the most obvious conclusion of this study is the inadequacy of the diet used in these cases and of that generally employed in typhoid fever."

There is, therefore, strong experimental and clinical evidence in favor of giving typhoid patients sufficient food to meet their demands for energy.

II. HOW MUCH FOOD MAY BE CONSIDERED NECESSARY TO FULFILL THESE REQUIREMENTS?

In answering this question I shall consider, first, the energy value of the food. The relative proportions of protein, fat and carbohydrate to be employed will be referred to later.

One of the chief characteristics of typhoid fever, as we know it, is emaciation (Fig. 1). Losses of 25 pounds during the course of cases of even moderate severity are not uncommon, and as much as 50 pounds may be lost by patients during prolonged, severe attacks. If these losses concerned only fat and water, they would probably not be serious, but they involve muscle and other tissues as well. Losses of from 15 to 20 gm. of nitrogen a day, representing from ½ to ¾ pound of muscle, are not unusual. Scarcely any one would deny that these losses should be prevented if possible, provided the means taken for their prevention is not more dangerous than the losses themselves. The hunger of many patients during the course of the disease and of all patients during convalescence is probably Nature's protest against the practice of partial starvation. Patients who are well enough complain of it, those who are too ill to complain probably have even greater need for food.

The loss of weight in typhoid fever has been attributed to two causes: to the temperature and to so-called toxic destruction.

The Temperature.—The belief is common, even among the laity, that fever burns up tissues. Fritz

Fig. 1.—Apparatus for weighing bed patients constructed by hospital carpenter. The height of the table when placed on scales corresponds with that of the bed. The legs of table which just clear the floor prevent tilting.

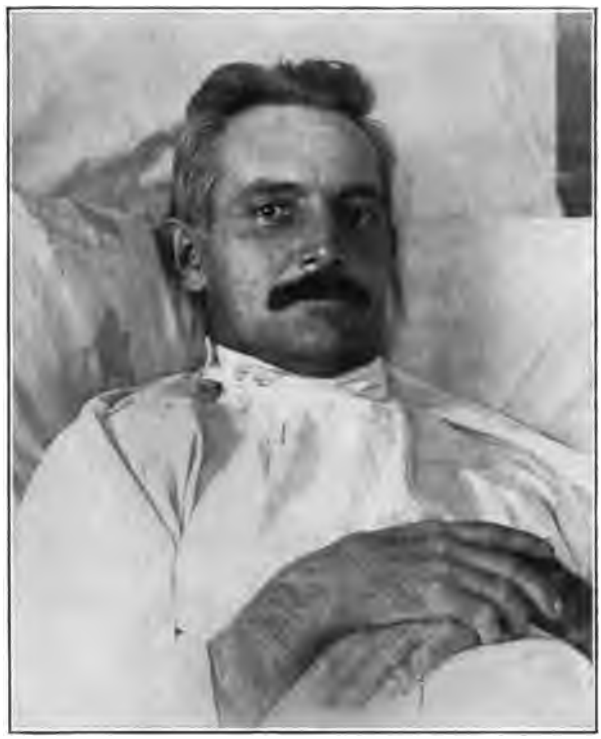

Fig. 2.—W. G. Blood culture positive. Very severe. Temperature 103-105 F. Duration of fever 47 days. Relapse of 27 day's duration. Ill for 3 weeks before admission. Said he had lost 15 lbs. Weight on admission, 151 lbs.; at end of first period, 140 lbs.; at beginning of relapse 144 lbs.; at end of relapse 140 lbs.; at first day up 154 lbs.; on discharge, 174 lbs. Picture was taken before patient was allowed out of bed.

Fig. 3.—J. C. Blood culture positive. Severe. Temperature 101-105 F. Duration of fever 21 days. Weight, 12th day, 60½ lbs. (2 days after admission); 16th day, 58 lbs.; 18th day, 59½ lbs.; 22d day, 59 lbs.; 26th day, 58 lbs.; 28th day, 60 lbs. Picture was taken before patient was allowed out of bed.

Fig. 4.—P. Z. Blood culture positive. Moderately severe. Temperature 101-103.8 F. Duration of fever 34 days. Weight 6th day, 129 lbs.; 10th day, 132 lbs.; 15th day, 136 lbs.; 17th day, 135 lbs.; 21st day, 133 lbs.; 24th day, 132 lbs.; 27th day, 132 lbs.; 35th day, 130 lbs. Picture was taken before patient was allowed out of bed.

Voit[15] and Linser and Schmid[16] have shown experimentally both in animals and man that pyrexia does increase metabolism. There is, therefore, a substantial basis for the common belief.

Toxic Destruction.—In addition to the febrile loss of body substances, there is a further increase in metabolism in the course of infective diseases which is due to the action of bacterial toxins. This is the so-called toxic destruction. The manner in which the toxins act is not definitely known.

Shaffer and I have found in our cases[17] that the losses due to both of these causes can be prevented by a high caloric carbohydrate diet. As no diet hitherto proposed for typhoid fever has furnished sufficient energy for the metabolic exchanges of the patient, we have concluded that the most potent factor in the losses of the disease is partial starvation.

We may calculate the minimum energy requirement of the typhoid patient as follows: A normal man at ordinary rest requires about 33 calories per kilo of body weight each day. According to Krehl,[18] the average typhoid patient requires a 25 per cent. addition to this in order to meet the febrile increase in heat production. This gives 41 calories per kilo of body weight per day or approximately 3,000 calories for a man weighing 150 pounds. It must be emphasized that this is the calculated minimum requirement.

If this calculation is approximately correct, then a patient weighing 150 pounds, taking 2 quarts of milk a day, is getting only 50 per cent. of his minimum requirement, and a patient of the same weight on a "liberal diet" is getting only 75 per cent. of this requirement. As a matter of fact, the discrepancies are even greater, since we found that the optimum requirement

15. Sitzungsb. d. Gesellsch. f. Morph. u. Physiol. in München, 1895, xi, 120.
16. Arch. f. klin. Med., 1904, lxxix, 514.
17. To appear in Arch. Int. Med.
18. Principles of Clinical Pathology, Hewlett translation, Philadelphia, 1905.

varied in different patients and at different stages of the disease, but was always greater than the calculated minimum. Our best results were obtained when the diets furnished from 60 to 80 calories per kilo per day, or 4,000 to 5,500 calories. In one case we reached 100 calories per kilo or 6,000 calories a day.

We have studied patients on a strict milk diet—2 quarts a day—and found that they lost from 5 to 12 gm. of nitrogen. These losses would cease, or at least be greatly reduced, when the energy value of the diet was raised. Forty-six patients altogether have been on our diet, with only one death. This was a case of ambulatory typhoid; the patient's pulse was alarmingly feeble on admission to the hospital, and he died a week later from what appeared to be acute dilatation of the heart. (I feel that this case might, with fairness, have been excluded from the total.) Many of the 46 patients suffered from very severe forms of typhoid fever. For example, the temperature ranged from 103 to 105 F. in one case and lasted 47 days, with a relapse of 27 days' duration. Some of the patients were kept almost in nitrogen equilibrium throughout the disease. It was not unusual for patients to weigh as much or even more when they were allowed to get up (usually about the fourteenth day of convalescence) as when they were taken ill. In one instance, the patient actually gained 2 pounds during a sharp relapse of 10 days' duration. In all instances, the patients appeared brighter and stronger and better able to fight the disease. The percentage of relapses was slightly lower than in another division of the hospital where the usual diets were employed. I do not feel disposed to make any statement as yet regarding the course and rapidity of convalescence. All of the patients left the hospital in excellent condition. Some of them I have been able to follow, and the impression I received was that convalescence progressed rapidly. But it is difficult to judge of this unless the

patient can be seen frequently, which is manifestly impossible in the case of hospital patients.

Since the calculated minimum requirement of 3,000 calories diminishes but does not prevent protein loss, I would answer the second question by saying that a patient of 150 pounds' weight should be given food equivalent to 4,000 calories a day, but that the greater the energy value of his food, provided his digestive organs can handle it, the greater will be the sparing of protein and other body substances.

Diet.—The diet we used consisted, in the main, of milk, cream, milk-sugar and eggs. In addition, we allowed small slices of stale bread or toast, with as much butter as the patient wished. The daily quantities of these articles of food were about 1½ quarts of milk, from 1 to 2 pints of cream, from ½ to 1⅔ pounds of milk-sugar and from 3 to 6 eggs. It will be necessary to say a few words about each of these articles.

Milk: I am convinced after much experience with it that milk, in moderate quantity, is not an undesirable constituent of the typhoid diet. When the quantity is excessive, it may unquestionably produce harm, but the argument that it forms an excellent culture medium for the typhoid bacillus in the intestine has been exploded by the investigations which have shown that typhoid fever is a bacillemia. Milk in the quantity mentioned has not produced tympanites in our cases. Occasionally milk curds have appeared in the stools and then the quantity of milk has been diminished or it was peptonized. A good average milk will furnish 740 calories to the quart.

Cream: Though cream furnishes a large amount of energy, it is not advisable, according to our present knowledge, to give more than one-third of the total calories of the diet in the form of fat. Fat in the food, if absorbed, will protect an equivalent amount of fat in the body. Fat protects protein also, but not so efficiently as does carbohydrate. Other objections to cream in large

amounts are its tendency to upset the stomach and to produce diarrhea. Patients usually can take a pint of cream a day without difficulty. We have given as much as 42 ounces. In only one instance has the cream disagreed. This patient developed diarrhea when the quantity reached a quart a day. The diarrhea stopped immediately when the cream was withdrawn. The cream supplied at Bellevue Hospital contains from 25 to 30 per cent. of fat and furnishes 1,300 calories to the pint.

Milk-sugar: Carbohydrate protects body protein better than any other foodstuff. For this reason a large proportion of the energy of our diet is supplied in that form. Starches can not be used in quantity because of their bulk and the consequent tax on the digestive organs. Therefore, it became necessary to select one of the sugars. We chose milk-sugar because it is not very sweet and not so likely to pall on the taste as other sugars, and because it does not so readily produce digestive disturbances. We have not found that it exhibited the laxative properties which have been ascribed to it; in fact, patients taking it often suffered from the constipation which is so common in typhoid fever.

The objections which we have found to milk-sugar are: some patients complain that it is too sweet; in some instances it produced nausea and vomiting, but more often vomiting without nausea, the stomach contents being simply regurgitated. When vomiting occurs, the milk-sugar should be stopped. As a rule, however, its administration may be resumed in smaller quantities after several days and the quantity then be gradually increased. In a few instances the milk-sugar has caused moderate tympanites. We have not had a patient who could not be educated to take it in sufficient amount to materially raise the caloric value of the diet. The method of giving the milk-sugar will be discussed later. Milk-sugar furnishes 4 calories for each gram, or 120 per ounce.

Eggs: While it has not been determined definitely how much nitrogen a typhoid patient requires in 24 hours, our results indicate that the optimum amount lies between 12 and 16 gm. One and one-half quarts of milk and a pint of cream furnish 11 gm. of nitrogen and we made up the deficit with eggs. A two-ounce egg supplies 1+ gm. nitrogen.

We chose eggs because they are easily digested and readily obtained. Meat and home-made meat juice are more likely to cause digestive disturbances. I have specified "home-made" meat juice because the consensus among scientists is that commercial meat preparations possess very little food value.[19]

It is important that the protein content of the typhoid diet be kept as low as is consistent with the nitrogen demands of the patient. In addition to digestive disturbances, the injudicious administration of meat may seriously disorder metabolism. It is well known that meat may cause the *febris carnis*. Ewing and Wolf[14] have recently found evidence in the urinary nitrogen to indicate that this "meat-fever" is due to the inability of the patient to digest and metabolize properly some alien proteins. They noted also in their cases this very important fact, that the *febris carnis* was soon followed by albuminuria, which, they suggest, may be the starting point of nephritis. Therefore, the caution may be repeated, to keep the protein content of the typhoid diet low during the disease and to allow meat sparingly early in convalescence.

Some Practical Considerations.—The diet which I have outlined is a difficult one to give to patients, on the whole rather more difficult than milk. Intelligent and reasonable persons, however, take it readily when the objects of the diet are explained to them. In other instances, patients are not told that the milk differs from what they have been accustomed to taking. The

19. Bull. No. 114, Bureau of Chemistry.

greatest difficulty has been experienced with adolescents who refused to take the diet because patients near them were allowed other food. When I have been convinced that the reason for not taking it was sheer stubbornness, I have insisted on carrying out the order. When I have even suspected that the diet was disagreeing with the patient, I have modified or stopped it, but always have cautiously resumed it (Figs. 2 and 3).

The food has been given at two-hour intervals, except that patients have not been awakened at night. The cream has usually been added to the milk, in the proportion of 2 ounces cream to 6 ounces milk, though a palatable ice-cream may be made with cream and milk-sugar. The milk-sugar should be given in small quantities at first—a tablespoonful to the glass of milk—and gradually increased to 4 tablespoonfuls. Many patients will take 2 ounces of cream, 6 ounces of milk and 2 ounces of milk-sugar several times a day, but this is a rich combination. At other times the milk-sugar may be given in tea, coffee, or cocoa, or it may be made with an egg into soft or baked custard. A milk-sugar lemonade may be given once or twice a day. If the water and sugar are boiled for two minutes before the lemon juice is added, 4 ounces of milk-sugar may be put into 8 ounces of lemonade. If the lemonade is not sweet enough, a tablespoonful of cane-sugar may be added. The eggs may be given soft boiled, soft poached or shaken up in milk, with or without whiskey.

While I believe that the foods mentioned must form the basis of the ideal diet for typhoid fever, much remains to be done in working out details. The greater the variety and the more palatable the dishes presented to the patient, the more content will he be to adhere to the prescribed diet. We have not yet been able to devote much time to the selection of variety in foods and dishes, but this is one of the questions which soon will engage our attention.

CONCLUSIONS

1. The practice of partial starvation, at present followed in the treatment of typhoid fever, is highly detrimental to the patient's welfare.

2. It is not only desirable but necessary that the typhoid patient be given sufficient food to cover his energy expenditures.

3. The amount of food required for this purpose will vary with different patients, but may be estimated approximately on the basis of 40 calories per kilogram of body weight per day.

ABSTRACT OF DISCUSSION

DR. MAX EINHORN, New York: The principles contained in the paper were recognized as far back as Graves, but they were not carried out as by Dr. Coleman. Since the days of Hippocrates it has been customary to subject these patients with fever to starvation diet, giving only water and barley-water, and under this rest treatment the patients felt quite comfortable; this method of treatment was carried out up to the time of Graves, who began to feed his typhiod patients with milk. The Hippocratic principle of rest was correct in caring for patients with diseases which run a short course, or last but a short time. Take an adult, with pneumonia, for instance, who is in good condition, the disease will last but five, six or seven days, the loss of a little flesh is not going to do him any harm; in starvation treatment may be carried out. The only important point that should be borne in mind and not forgotten is that these patients should have plenty of water. Individuals may go without food for a short time, but they can not stand the loss of water for even five, six or seven days. They can stand twenty days, loss of food, provided they are given plenty of water. But if we extend this principle a little further to patients with typhoid fever we then begin to see harm in the system. Typhoid fever lasts two, four, five or six weeks, and if we try to extend that principle the organism loses too much and irreparable consequences result to the system caused by the great loss of flesh. For that reason Graves believed that these patients should not be starved; he believed that they should receive nourishment and that one of the best substances for this was milk. Since then milk has been given to patients with typhoid fever, except perhaps when some fanatics give the starvation treatment. Twenty-five years ago, when I was house physician in a hospital, patients with typhoid fever were given a diet consisting particularly of milk, broths and raw eggs. Ten ounces every two hours were given, and also plenty of water and lemonade. With that diet, although we

could not keep up the weight, we did prevent some loss. We gave occasionally a soft diet and farinaceous foods. What is new in Dr. Coleman's report is that he has succeeded in checking this loss of weight during the typhoid fever period. That has not been done before. During that period the organism requires more and more calories to replace the loss caused by the increased oxidation; the patient requires forty instead of twenty-five or twenty-six calories. Dr. Coleman has succeeded and we must follow his example and feed patients suffering with typhoid fever.

DR. THOMAS A. CLAYTOR, Washington, D. C.: For five or six years I have been feeding my typhoid fever patients along the lines advised by Dr. Shattuck and I agree with Dr. Coleman in his statement that when a physician has once fed these patients he will never be likely to return to the starvation diet. I believe that typhoid fever patients are more likely to recover when fed than when starved. They are far more contented. One of the most trying experiences with which these patients have to contend is hunger. When fed they are comparatively happy, they are much stronger, they convalesce more rapidly. Instead of being reduced to skin and bones they get up in good physical condition and are able to return to work much earlier, which, to the working man, is a very important thing. I certainly have not seen any more instances of hemorrhage or of perforation among the patients liberally fed than in those on liquid diet. I feel convinced that within the next ten years liberal feeding will become the rule rather than the exception in the treatment of typhoid.

DR. ARTHUR K. STONE, Boston: In a series of over fifty typhoid patients treated by me last summer at the Massachusetts General Hospital the diet used was much more mixed than that used by Dr. Coleman and was the diet suggested a number of years ago by F. C. Shattuck. It represented about 2,000 calories and my patients did as well as did Dr. Coleman's; there was only one death in the series. On the whole, the patients behaved very well on that diet and lost but little weight, but I debated whether it would not be wiser to add sugar of milk or in other ways to increase the caloric value of the diet; but as they were doing so well I concluded that this would not be necessary. However, to make sure, I invited Professor Follin to see these patients with me, requesting him to suggest whether it would be wise to increase the caloric value of the diet. He said he saw no reason why I should change from the diet I had been using. Practically no drugs were used in the treatment of these cases and the baths were light sponges.

DR. A. JACOBI, New York: Dr. Coleman is to be congratulated on his results, which, with that diet, I should not expect. I am greatly astonished at the good results he obtained. His diet was milk and, I hope, good milk. He has been

very fortunate and I have not the slightest doubt the patients did very well; but what he told us certainly does not agree with what we know. It looks almost impossible to expect a healthy person, far less one with typhoid fever, to digest as much food as his patients did. I have never seen more disorders of digestion with indicanuria, acetone and diacetic acid in the urine than in patients who consumed a great deal of fat in that shape. Moreover, his patients taking so much fat took, at the same time, much milk undiluted and unmixed; my patients could not take it without becoming ill. I know that few children will stand an exclusively milk diet very long. It is true that patients will stand a great deal, but we should not contribute to their suffering. I wish to state that it is impossible for an average intestine to digest an unmixed cream to that extent. We cannot go into the physiology of digestion at this time, but I know that both adults and children, healthy or diseased, will bear milk that is diluted with cereal better, particularly in fevers in which the gastric secretions are lower than before the individuals were taken ill. In typhoid fever I would rather furnish the patients with 2,500 calories than 3,000, 4,000 or 5,000. It seems to me that Dr. Coleman, in his good wishes for the patient, has gone too far. Yet he says he has lost but one patient, and I think that other conditions in the hospital must have been extremely favorable and the patients well cared for. I congratulate him on his results, but I wish to give warning that we should be very careful in fat feeding to the extent that he has proposed to us. If a cereal is mixed with the milk, it will be more digestible. For many years I have not given pure milk in typhoid fever; I always mix it with rice-water or barley-water or other cereals or gelatin. I may not agree with Dr. Coleman's views, but I cannot gainsay his results, which are almost unprecedented. What I have said, however, is intended as a warning only.

Dr. James M. Anders, Philadelphia: I think it is a significant fact that general practitioners no longer pursue a starvation diet in the treatment of typhoid. Certain dietetic principles should be kept in mind in connection with the management of typhoid fever, and this remark applies to other infections as well. First of all, we should consider the proteid substances and recollect that the energy they represent is not all utilized by the system. For example, too much proteid food favors putrefaction in the intestinal tract, and with this there is brought about increased gravity of the case, especially in the direction of local symptoms. On the other hand, we should recollect that the energy represented by carbohydrates and fats is entirely utilizable within the system; therefore, we should give a certain amount of carbohydrates and fat to typhoid patients. This is what Dr. Jacobi has just hinted at in connection with the giving of milk. It should be remem-

bered that one object of the dietetic treatment is the preservation of the tissues of the body and the prevention of emaciation which would otherwise occur. Fats, however, will not do this, but the carbohydrates will do it. Some of Dr. Coleman's success in maintaining the bodily weight of his patients so well may have arisen from the use of carbohydrates which were easily digested, and particularly the milk sugar which he recommended. It seems to me that his main suggestions are excellent ones and could be profitably followed by the general profession. The preservation of tissues, however, can only be accompanied by the use of carbohydrates.

DR. JAMES B. WALKER, Philadelphia: I have been very much interested in Dr. Coleman's paper because I have feared that increase in feeding of typhoid-fever patients may go too far to the other extreme. I believe that Dr. Coleman's results are thoroughly honest and true, but I fear, with Dr. Jacobi, who is always right, to give as much cream to a typhoid patient as Dr. Coleman has done. One article of diet which I think should not be given is starch. Starches are digested in the small intestine largely, as in the absence of chewing, insalivation is almost *nil*. Those who advocate a crust of bread or toast or other starchy food make a mistake in that they throw work on a part of the bowel that is not prepared to do it. I have found calves'-foot jelly—freshly prepared from the calves' feet and not made from the gelatin of the shops too often containing the clippings from tanneries—an appetizing and digestible addition to the typhoid diet. I should like to add this to Dr. Coleman's list. I have given as much as one pint daily. As gelatin is believed to be antehemorrhagic, it may help to avert this dangerous complication. I want to advise against the use of starches for what seems to me good physiologic reasons, to advocate the use of calves'-foot jelly as an addition to the diet, and to protest against too varied and liberal feeding of patients affected with typhoid fever.

DR. D. L. PARKER, Detroit: The tendency to more liberal feeding in typhoid is establishing itself rapidly, and it seems to me that the principle that underlies the whole scheme is the return to the mode of living which is natural to the patient, so far as his condition will permit. Certain articles of diet must be eliminated, such as starches, which are digested in the small intestine, as Dr. Walker stated. One of the most important things to remember is that the natural diet contains salt, and, as a rule, the diet given to patients with typhoid fever contains very little salt. For a number of years it has been my practice to see that these patients receive as much salt at least as on an ordinary diet. Another important thing is to have sufficient time between the feedings. It has been found in the forced feeding of tuberculous patients, for instance, that the taking of food at intervals of four or five hours is very much better for these patients than if the

meals are closer together. No person here in this room would think of taking food every two hours. I think the giving of food should be at longer intervals. Sufficient time should be given for the digestion of one meal before another is given.

DR. WOODS HUTCHINSON, New York: Nothing illustrates the progress of medicine better than the treatment of typhoid fever. Over sixty years ago Graves of Dublin chose as his epitaph "He fed fevers." Prior to this, blankets were placed over these patients, they were given very little food; even with high temperatures they were not allowed much water and no fresh air; the windows were kept closed; cold water to drink was regarded as deadly; and only lukewarm slops were permitted; in fact, the patients suffered almost as much from what was done for them as they did from the disease. Six years ago I began to use a liberal diet in my cases of typhoid fever, and the results have been the same as Dr. Coleman's. I had not the courage to carry it so far as Dr. Coleman has done, but the patients were given an abundance of tender meat, broths, jellies, crackers, toast, ice-cream, etc., and the results were excellent, not only as to keeping up the weight and strength of the patients, but also in preventing that condition of collapse after the fever subsided and the violent convalescent appetites which hitherto had craved such things as corned beef, beans and cold slaw. The patients made more rapid recoveries, had fewer complications and the results as a whole were very good. We think too much of the risk to the damaged intestine from liberal feeding in this disease, and regard typhoid fever as an intestinal disease too exclusively. Typhoid is a general disease, and, as has been shown, those patients who have been fed liberally, instead of suffering more from putrefactive changes in the intestines and tympany, have less of these changes, and fewer complications than those who are underfed. We are coming to see that many of the later symptoms that occur in the disease are due not so much to the actual toxic products of the bacilli as to the poisons generated from the broken-down tissues of the patient. Many of the symptoms occurring late in typhoid fever and due not so much to the disease itself as to the mistaken method of treatment, among which starvation ranks high. There is a risk in withholding food as well as in giving it.

DR. WARREN COLEMAN, New York: I did not foresee the nature of the questions which have been asked me or I should have requested more time of the chairman for my paper. One cannot deal adequately with such a subject as diet in typhoid fever in ten minutes. For lack of time I cannot answer all the questions that have been raised in the discussion. I feel, however, that I must attempt to reply to Dr. Jacobi.

The first thing I would say, and say emphatically, is that I did not experiment with patients in a way that was not thor-

oughly justifiable. Every increase made in the amount of milk-sugar was carefully controlled by observation in the hospital and by examinations in the laboratory of experimental pathology. Every increase made in the amount of fat was controlled in the same fashion. When there was reason even to suspect that the food was not agreeing with a patient, that particular article of food was stopped or diminished in quantity. I think that Dr. Jacobi perhaps has gained a wrong impression with regard to the amount of cream given. The usual quantity was one pint; sometimes as much as a quart; and in one or two instance even more. I did not observe any digestive or intestinal disturbances in any patient who was fed on this relatively large amount of cream except once; diarrhea occurred in that instance. The cream was stopped and at once the diarrhea ceased. Cream was not given again to this patient. The stools of all the patients were watched very carefully. There was no evidence that the cream was not, for the most part, utilized.

I am convinced that the principal question regarding the typhoid diet is whether it is desirable to let a patient live on his own tissues when it is possible to protect his tissues by giving him enough food. I have not yet worked out all the details of the diet. It has been estimated that gelatin may replace protein to the extent of one-fifth of the daily need of nitrogen. I started out to determine whether by giving a patient a sufficient number of calories to cover his expenditures, I could protect the body tissues. This was accomplished. In future I shall work in part on more practical problems, such as the varieties of food which may be given and the proper ways to prepare them. I did not follow the plan of giving large amounts of water, but was guided chiefly by the desires of the patients.

The patients are weighed on a long table, which, when placed on the platform of the scales, corresponds with the height of the bed. The weight is obtained without more disturbance to the patient than moving him from one side of the bed to the other.

CHRONIC INFECTIOUS ENDOCARDITIS

FRANK BILLINGS, M.D.
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Bacteriemia now is recognized readily by means of blood cultures and a blood culture in febrile patients has come to be a not unusual routine in many hospitals. The technic is so simple that it may be successfully done at the bedside in private practice and the culture media may be transported a considerable distance to the laboratory. With a sharp hypodermic needle the blood may be withdrawn from a prominent subcutaneous vein without noteworthy pain or danger. The blood culture enables one to recognize more readily the infectious character of the disease. With an infection proved, the interpretation of the physical and clinical phenomena becomes rational. On this a definite diagnosis may be made and the prognosis becomes more certain. The treatment necessarily becomes more definite, rational and conclusive.

Before the use of blood cultures infectious endocarditis, termed malignant, ulcerative, etc., was sometimes recognized during life by the signs of local heart lesions, petechial spots of the skin, emboli of larger vessels, splenic enlargement and tenderness, microscopic and sometimes macroscopic hematuria, subcutaneous, often painful, reddish nodules, a not infrequent cough with or without bloody sputa, a septic temperature, sometimes very mild, at other times severe, rapid heart action, and, finally, a failing heart with dyspnea, cyanosis and death.

Every practitioner, especially if he has opportunities for hospital observation, has seen many patients suffering from what he believed to be infectious endocarditis, but has been unable to prove the diagnosis during life, and frequently a postmortem was not permitted.

In the patients who suffer from an infectious endocarditis implanted on an old lesion the clinical phenomena which are present even when first seen are those of broken heart compensation. There may be a septic temperature of moderate degree. The pulse may be that of ordinary broken heart compensation. There will be evidences of a widely dilated heart, cyanosis, a swollen, tender liver and more or less anasarca. The infectious nature of the condition could not be positively recognized without a blood culture.

Since blood cultures have been practiced the literature abounds in reports of infectious endocarditis, both chronic and acute. In many instances reports are made of cases in which the infectious organism was demonstrated during life by blood cultures, and in many others the inference is made that the disease was an infectious endocarditis because of the symptoms and the clinical course, but no positive evidence is furnished by blood cultures or by postmortem.

The series of cases on which this report is based have been proved by blood cultures made in all but one instance during life to be of infectious type. In one the bacterium was obtained immediately after death by paracentesis of the heart and the culture grown from the blood so obtained.

Only one acute case is included in this series and that one because it affords means of comparing the clinical course of the acute with that of the so-called chronic cases.

Osler[1] gives a classical description of chronic infectious endocarditis with a report of a series of ten cases. In the majority of the cases reported by Osler the disease extended over a long period; the shortest four months and the longest thirteen months. As stated by him, the disease may be manifested by a slight feverish condition only and may be prolonged for weeks or months. I think other symptoms usually are present, but escape notice because no definite observations are made of such patients. The cases are often mistaken for colds or beginning tuberculosis, and for various other conditions which are often thought to be simple and unimportant. Many suffer from chills of varying severity, coming on at irregular times and followed by fever and sweat. It is not strange, therefore, that malaria is considered the cause in many instances, and quinin may be given for a considerable period of time without benefit.

In infectious endocarditis, especially of the chronic type, occurring in those patients who have not suffered from a chronic valvular disease or other anatomical lesion of the heart, the symptoms may be mild, like those given by Osler and observed by many clinicians.

In the series of fourteen cases presented in this report the disease manifested itself clinically over varying periods of time. In one patient (Case 1) the symptoms began two years before the real condition was

1. Osler, W.: Quart. Jour. Med., 1909, ii, 219.

recognized. Case 8 began fourteen months before a definite diagnosis was made. Patient 13 probably suffered from the disease for more than two years, and in the earlier part of the illness the diagnosis of typhoid fever was made for a condition which was, in all probability, infectious endocarditis; the diagnosis having been based on the fact that there was fever and splenic enlargement. No rose spots were found, however, there was no diarrhea, and the Widal reaction was negative throughout. The shortest clinical course was that in Case 5, and even in this there is doubt whether the infection did not occur long before. Because of the long clinical course of many of the cases one is justified in the term "chronic infectious endocarditis."

Another important characteristic of such patients is the fact that they are ambulatory in many instances. Patient 7 unquestionably suffered from an infectious endocarditis for more than a year before she finally became bedridden and during that time traveled extensively. She was ill, as manifested by a poor appetite, languor, nervousness and a slight rise of temperature. Patient 6 was a student in a university when the clinical course evinced important illness, and for two months after leaving the university, while she remained ill, she was up and about and finally traveled by rail for the consultation, when her real condition was recognized. Patient 8 traveled from Iowa to Chicago suffering from dyspnea on exertion, general weakness, nervousness, palpitation of the heart, and so forth, and had been in a condition quite as bad, from the account given by her, for a year. Patient 10 was ill for three months before his condition was recognized, and in that interval traveled extensively and was off on a vacation, hunting and fishing.

While the disease did not produce conditions severe enough to force the patient to go to bed, yet if any one of these patients had been under daily observation there would undoubtedly have been found physical evidences of the disease sufficient to have required bed treatment.

I have personally studied the fourteen cases included in this report. The number could be made much larger by the inclusion of cases seen but once, or under conditions which did not permit of study of the patients or of the causative bacteria. The infectious organism found in these fourteen cases was as follows: [2]the pneumococcus (eleven cases);

2. During the period of time covered by this report cases of acute infectious endocarditis due to staphylococcus (one case), gonococcus (one case) and streptococcus (two cases) have been seen but are not included because of the acute clinical course.

streptococcus (three cases). The large proportion of patients suffering from pneumococcus infection as compared with streptococcocus infection is noticeable, even in so small a group of cases. This especially is true when compared with the report by Dr. Thomas J. Horder on Infective Endocarditis.[3] In his report the number suffering from pneumococcemia was less than one-third of those suffering from streptococcemia.

In communicating with clinicians in various cities I find that they report streptococcus infection of the endocardium to be much more prevalent or frequent than pneumococcus infections. Dr. E. C. Rosenow[4] has made the bacteriologic investigations in these patients. He has already made a report[5] on the cultural characteristics and the results of animal experiments with the pneumococcus found in these patients.

The organisms obtained in the eleven patients suffering from pneumococcemia had many of the morphological characteristics of streptococci. Study of the organisms in culture and in animals proved that they were the pneumococcus. In the three patients included in this series the study of the organism which was called the streptococcus was not afterward made as in the other patients, and it is the belief of Dr. Rosenow that, had the organism of these three patients been studied as in other cases, all would have proved to be the pneumococcus.

PNEUMOCOCCUS CASES: CHARACTERISTICS OF ORGANISMS ISOLATED FROM THE BLOOD OF THE ELEVEN PATIENTS OF THIS SERIES

The cocci all produced fine colonies in blood-agar plates surrounded by a variable zone of greenish discoloration. Hemolysis did not occur. When grown in isolated colonies on the surface of the blood-agar slants they all had a greater or lesser tendency to adhere tightly to the surface. The more chronic the case and the later in the course of the disease the organism was isolated, the more marked was this tendency of the organism to adhere to the surface of the medium.

Unlike the ordinary pneumococcus found in pneumonia, the organism grows readily in the fibrin clot of the broth of the blood culture in large clumps or colonies. The fluid portion often remains perfectly clear for

3. Hordes, T. J.: Quart. Jour. Med., ii, 289, 1909.

4. The Dane Billings Fellow in Medicine in Rush Medical College and a worker in research in the Memorial Institute for Infectious Diseases, Chicago.

5. Rosenow, E. C.: Jour. Infect. Dis., vi, 245, 1909.

twenty-four to forty-eight hours, after which time a diffuse or flocculent cloudiness appears, and an abundant sediment, which consists of masses or clumps of bacteria, precipitates. The organism is Gram-positive, usually is not surrounded by a capsule, and, when grown in broth or litmus milk, it forms diplococci with many very long conglomerate chains.

In the beginning it usually ferments inulin slowly, but this property soon is lost.

After cultivation on artificial media, usually it promptly loses the property of adhering to the surface, and later ceases to grow in chains and reverts to the characteristics of the typical pneumococcus. On passage through animals it often reverts very promptly to the type which is characteristic of the ordinary pneumococcus.

When first isolated they were all freely susceptible to phagocytosis in normal blood, and also in the patient's blood.

Cultures from all patients show a characteristically low grade of virulence to animals. Before the tendency to adhere to the surface is lost a primary injection of a huge dose intraperitoneally, intravenously or subcutaneously, or in all three places at once, is apt to produce endocarditis and pericarditis, but not peritonitis or subcutaneous abscesses. The tendency to produce endocarditis and pericarditis is very striking in all the animal experiments, quite regardless of the point of inoculation.

After the tendency to adhere to the surface is lost huge doses are practically never fatal, nor is endocarditis or pericarditis produced by the inoculation unless combined with injury of the endocardium, and then only rarely. Instead of rendering the animal more resistant to subcutaneous injections, as is the rule with the pneumococcus, injections of the modified strain render the animal more susceptible. After the second or subsequent injection several things may happen. First, the animal may die in a few days of a pneumococcus. The culture from the dead animal's heart blood resembles ordinary virulent pneumococci. Second, pericarditis and endocarditis, or pericarditis alone, may occur; and the characteristics of the organism obtained from the dead animal more nearly resemble those of the inoculated bacterium than of the ordinary pneumococcus. Third, in two instances, after two and three weeks respectively, the animals died of pneumonia, and the isolated organism from the dead animal resembled typical pneumococci.

This description corresponds in some respects with the statement made by Dr. Horder[6] in which a typical form of streptococcus is described by Dr. H. Thursfield.

It is to be hoped that others may study the streptococcal forms obtained from the blood in infectious endocarditis and other conditions as has been done by Dr. Rosenow. It may result in the establishment of the fact that the pneumococcus is the most frequent infective agent in endocarditis.

THE SOURCE OF INFECTION.

This may in some instances be satisfactorily learned. In one patient of this series the infectious endocarditis followed pneumonia. Tonsillitis had occurred in two. Alveolar abscesses occurred in two; grip occurred in one. In the other patients the source of infection could not be learned. There can be no doubt whatever that simple local infection, like tonsillitis, as well as abscesses of the aural cavities, infections of the postnasal space of the antra, and so forth, may be the port of entry.

In some patients of this series the infection was implanted on an old endocardial or valvular scar. An old heart lesion existed in seven patients, of whom six had suffered from rheumatic fever and one from chorea. Two of the patients gave no history and the question of previous heart lesion was in doubt. In five the infection had apparently been implanted on a normal endocardium or valve.

The valves involved in the fourteen cases were as follows: aortic valve alone, one; mitral alone, seven; pulmonary semilunar alone, one; aortic and mitral together, five; mitral and tricuspid together, one.

The evidence of heart lesion, as manifested by murmur, may be absent in the primary cases during the earlier part of the disease, and sometimes throughout it. Case 8 was examined by very competent physicians for months before the diagnosis was made and no heart murmur was heard. Case 10 had no murmur until about one month preceding death.

Pneumococcal inoculations with dead organisms were used with many of the patients and a careful study was made of the ordinary corpuscular elements of the blood, of the opsonic index, and of phagocytosis. It was found, among other things, that this organism apparently immunized

6. Horder, T. J.: Quart. Jour. Med., ii, 300, 1909.

itself against the antibodies of the host, a principle of infection first suggested by Prof. W. H. Welch. After inoculation leucocytosis was usually increased and phagocytosis was marked. The bacteriolytic power of the serum and of the leucocytes was, however, very low. The opsonic index was always increased by the injection. In some instances the temperature of the patient became lower after the inoculation, but the physical symptoms did not improve. In some patients, after inoculation with a large dose, the clinical course was aggravated in every way by the inoculation. In Case 10 the patient was inoculated several times with dead autogenous organisms with the usual results. When the patient was injected with normal serum intravenously, a sharp reaction followed, manifested by chill and fever, and the number of bacteria in the blood was much less for a period. No permanent benefit resulted from the attempt to furnish complement by the injection of normal serum. Two of the patients suffering with streptococcus infection were injected with antistreptococcus serum: Patient 11 with two, and Patient 9 with many, injections without benefit.

The prognosis, with the present knowledge or want of knowledge in reference to any specific treatment, is, in my experience, bad.

The treatment should be absolute rest, with good air, sunshine, as much simple liquid and soft solid nourishment as may be given, and the use of those remedies which will conserve the patient's strength and the functions of the organs without too much mischievous interference. Inoculations of patients with large doses of their own dead pneumococci was always harmful. Observation of patients injected with even small doses (2,500,000) leads me to believe that this form of treatment for infectious endocarditis due to the pneumococcus is not only devoid of benefit to the patient but probably is harmful.

PROTOCOLS OF CASES

CASE 1.—D. R., male, single, aged 18, American, was admitted to the Presbyterian Hospital, Feb. 27, 1904; died March 31, 1904. Autopsy. Diagnosis: Chronic infective endocarditis, pneumococcemia, mitral stenosis and regurgitation.

History.—At 5 years old the patient had an attack of acute rheumatic fever; when about 10, a second attack of rheumatic fever. In the interval between the two attacks of rheumatism he was at times confined to bed with dyspnea and rapid heart action. During the second attack of rheumatism he was also troubled with dyspnea to the degree of orthopnea. From 11 to 15 years of age he was free from illness but noticed dyspnea on exertion. At 15 years of age he was

confined to bed with an attack of weakness of the heart manifested by rapid heart action and dyspnea. The present illness began at about 16 years of age, that is, two years before the patient came under observation, with an attack of what was called grip. This seizure was ushered in with a cold in the head, anorexia, nausea and vomiting, shortness of breath and orthopnea. During the two years he has been constantly ill, confined to the bed most of the time, disturbed by nausea and occasional vomiting, rapid beating of the heart, dyspnea, more or less cough, and lately most of all if he attempted to exert himself, and also when he attempted to lie down. He was always most comfortable when sitting. No authentic history could be obtained of his pulse, temperature or respirations during this illness.

Examination.—On admission the patient showed marked pallor of the skin and mucous membranes. There was a slight blueness of the finger-nails and visible mucous membranes. The patient's general nutrition was below par. The tongue was grayish white; the tonsils somewhat enlarged and red. The respirations were increased but not labored. A marked precordial pulsation with systolic retraction was visible. There was one hazelnut-sized lymph gland in the left submaxillary region. No other lymph nodes were noticeably enlarged. Palpation over the chest showed a marked tremor in the region of the heart but no thrill. The left border of the heart extended 15 cm. from the mid-sternum, the right 5 cm. to the right of the sternal edge and the base was at the second costal cartilage. The apex-beat was in the sixth interspace just outside the nipple line. The heart action was rapid and of the gallop-rhythm type. Many heart pulsations did not reach the radial arteries. There was a loud musical systolic murmur heard in the mitral area and also in the left axilla and over the left scapula. There was also a very rough presystolic murmur heard in the mitral area and toward the sternum. The pulmonic second tone was markedly accentuated. There was no pulmonary dulness. The breath sounds were harsh and numerous mucous râles are heard on both sides, especially at the bases. The abdomen was flat and the abdominal walls thin. The liver did not extend below the costal arch and the spleen was not palpable. There was no edema of the extremities. The urine was scant, heavy, contained much lateritious deposit with a trace of albumin and a few hyalin casts and many moderately motile bacilli. On March 1 a twenty-four collection showed 600 c.c., specific gravity 1.032, a trace of albumin, a few hyalin and granular casts and many urates.

Course of Disease.—The patient had a septic temperature ranging from 99.2 in the morning to 101 or 102 in the afternoon. He gradually became worse, compensation became broken and venous stasis gradually developed with edema of the lower extremities, transudation in the serous cavities of the abdomen and chest and coincidently greater cyanosis. A blood culture revealed the pneumococcus in pure culture. In the latter part of the patient's illness he became drowsy and finally passed into coma. Cough, which existed from the first, became worse and the sputum became blood-stained. Areas of dulness developed over the lungs indicative of infarcts. The blood examination showed 5,500,000 red cells, 95 per cent. hemoglobin and 25,000 leucocytes on admission, and the leucocytes remained high throughout the illness of the patient. The patient died on March 31, 1904, and an autopsy was made a few hours thereafter.

Anatomical Diagnosis.—Chronic mitral endocarditis with calcification and stenosis of the mitral orifice; chronic mural endocarditis of the left auricle;

fibrous adhesive pericarditis; acute vegetative aortic and tricuspid endocarditis; cardiac hypertrophy with dilatation, especially of the left auricle; recent pulmonary infarcts of both lungs; terminal pulmonary edema with abscesses in the right middle lobe; passive hyperemia of liver, spleen and kidneys; hydroperitoneum; left hydrothorax; general edema; right serofibrinous pleuritis; caseous tuberculosis of tracheobronchial lymph glands.

Cultures made from the heart's blood and vegetation on the aortic and tricuspid valves revealed the pneumococcus in pure culture.

CASE 2.—Mrs. C. P., housewife, aged 22, was admitted to the Presbyterian Hospital March 5, 1904; died March 19, 1904. Autopsy. Diagnosis: infective endocartis, pneumococcemia, mitral stenosis and tricuspid insufficiency.

History.—Patient stated that she always had enjoyed a fair degree of health but had never been robust. Five years before coming under observation she suffered from an attack of grip, and from that time dated the beginning of her present illness. She never fully recovered her health and complained of shortness of breath on exertion, palpitation of the heart and general weakness. These symp-

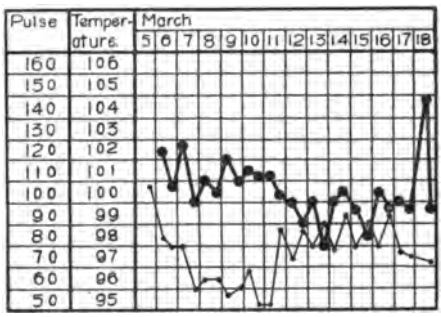


Chart 1.—Pulse and temperature curves in Case 2. Heavy line indicates pulse; fine line, temperature.

toms gradually increased and for the past four months she had not been able to work. Edema occurred in the legs, which were more swollen during the day, and the face was swollen early in the morning. She suffered from a miscarriage four months before admission, and following this the edema appeared, with greater shortness of breath, which was aggravated on the slightest exertion. Cough had developed in recent time and was troublesome enough to keep the patient awake at night.

Examination.—On admission the patient sat propped up in bed. The face was flushed and there was a slight cyanosis of the skin and visible mucous membranes. Respirations were 30 to the minute. The throat was red and cyanotic but the tonsils were not enlarged. The resonance of the chest was normal and a few dry and moist râles were heard over both sides of the chest, especially at the end of deep inspiration. The apex-beat of the heart could not be seen but was palpable in the fifth interspace just within the mammillary line. There was a faint systolic thrill. Dulness extended on the left 11 cm. from the midsternum

to the second left rib above and to the right edge of the sternum on the right. There was a loud rough systolic murmur in the mitral area with a marked accentuation of the second pulmonic tone. The pulse was very small and rapid, 110 to the minute. The abdomen was full, the abdominal wall tense and tenderness existed over the upper portions. The liver and spleen could not be palpated. A soft edema of the lower extremities extended to the knees. The finger-nails were cyanotic and the finger-ends slightly clubbed. The blood examination showed, red cells, 5,100,000; hemoglobin, 92 per cent.; leucocytes, 8,300. Twenty-four-hour urine amounted to 400 c.c.; specific gravity, 1.014; urea, 3 per cent.; trace of albumin and a few hyalin and faintly granular casts. The patient's temperature was of a low septic type ranging from subnormal to about 99 in the morning to 100 to 102 in the afternoon. (See Chart 1.)

Course of Disease.—Gradually the heart inadequacy increased with greater dyspnea, cough and more marked evidences of venous stasis. On March 17 the patient complained of pain in the liver region which could be felt extending downward to the level of the navel and was markedly tender. A pleural friction was heard over the left lower lobe posteriorly. On March 19 a loud diastolic murmur could be heard in the mitral area. A blood culture showed the pneumococcus in pure culture. The patient died on March 19, 1904, and an autopsy revealed the following:

Anatomic Diagnosis.—Mitral stenosis; vegetative tricuspid endocarditis; hemorrhagic infarcts and hyperemia of kidney, lungs, spleen and liver; hydropericardium; hydrothorax; anasarca; localized left fibrinous pleuritis.

Bacterial examination of the blood from the heart, from the lung infarcts and from the vegetations on the tricuspid valves revealed the pneumococcus in pure culture.

CASE 3.—Miss A. S., aged 15, was admitted to the Presbyterian Hospital, May 6, 1904; died June 6, 1904. Diagnosis: infective endocarditis, pneumococcemia, mitral stenosis and regurgitation.

History.—Patient's previous health was good. In February, 1903, she suffered from an attack of pneumonia. She was confined to bed for a month and never regained her strength. During the last year she had not been able to work, and much of the time had been confined to bed because of general weakness, dyspnea on exertion and palpitation of the heart. All of these symptoms had increased gradually and recently the patient had coughed a great deal.

Examination.—On admission the patient's face was flushed, slightly cyanotic. The visible mucous membranes were cyanotic. The veins of the neck were slightly enlarged and pulsating. The whole anterior chest heaved with each heart-beat. The heart action was tumultuous and irregular. Respirations were rapid and labored. The lung resonance was practically normal with relative dulness posteriorly and below. The breath sounds were harsh, expiration prolonged and a few moist râles were heard over the dependent portions of the lungs. The heart extends to the left 18 cm. from the midsternum, to the second left rib above and 5 cm. from the right edge of the sternum. The apex impulse was diffuse in the sixth interspace outside the mammillary line. A distinct tremor could be felt over the apex impulse. A loud, rough, double murmur could be heard; the systolic murmur transmitted far to the left. The second pulmonary tone was much

accentuated. A soft systolic murmur could be heard over the right fourth and fifth intercostal spaces. The abdomen was distended; the liver large, somewhat indurated and very tender. The spleen was not palpable. There was slight edema of the ankles and feet. Blood examination, 5,200,000 red cells, 100 per cent. hemoglobin, 15,000 leucocytes. Blood culture on admission was negative. On May 19 the leucocytes were 25,700, and a blood culture was negative. Urine on admission was scant, specific gravity 1.025; it contained a trace of albumin and a few hyalin and granular casts.

Course of Disease.—The temperature throughout was of a septic character. The patient grew rapidly worse, there were increasing evidences of heart inadequacy manifested by greater dyspnea and cyanosis; edema of the lower extremities gradually increasing to general anasarca; cough with bloody sputum and evidences of consolidation of a part of the right lower lobe. The patient died of exhaustion on June 6, 1904, and an autopsy was not obtained.

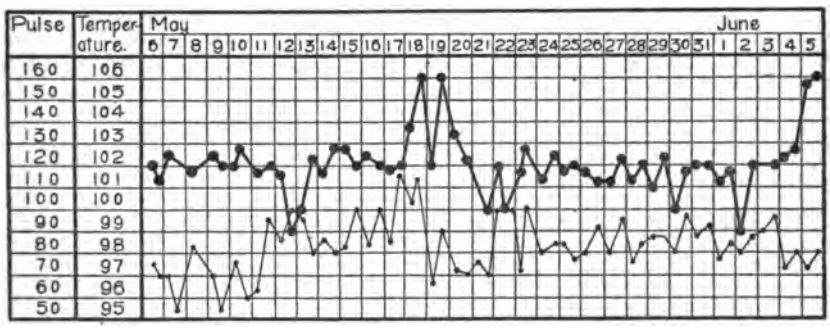


Chart 2.—Pulse and temperature curves in Case 3. Heavy line indicates pulse; fine line, temperature.

Puncture of the heart with precautions as to cleanliness was made immediately after death, and from the heart's blood a pure culture of the pneumococcus was obtained. The temperature throughout was of a septic character. (See Chart 2.)

CASE 4.—F. L., male, single, aged 16, Italian, admitted to the Presbyterian Hospital, Chicago, March 21, 1904; died April 13, 1904. Autopsy. Diagnosis: infective endocarditis, streptococcemia, mitral stenosis and aortic insufficiency.

History.—The patient said that his only previous illness was an attack of chorea which occurred six years before admission. Since that illness he had never been quite well and had suffered from dyspnea on exertion and some palpitation of the heart. He had smoked cigarettes to excess until seven months before admission. The present illness dated, the patient thought, from the time he had chorea; but in spite of lessened strength and endurance, more or less palpitation of the heart and shortness of breath, he continued his work until one year before admission. Then these sysmptoms increased to such a degree that he was

obliged to discontinue work. During the last year he had been confined to the house sitting in an easy chair or confined to bed. He had suffered a good deal from indigestion manifested by heaviness after meals and eructation of gas. A month before admission he noticed for the first time that his feet were swollen, and two weeks later this swelling rapidly extended to the thighs, then to the scrotum, and finally to the abdomen. He had had cough with some blood-streaked sputum, had been short of breath, especially on the least exertion and had noticed also a very rapid and throbbing heart action.

Examination.—On admission the patient is in orthopnea with rather marked dyspnea which was increased on the least exertion. The lips and skin were slightly cyanotic and pale. There was distinct pulsation of the distended veins in the neck. The general nutrition was poor. The lung resonance was practically normal and auscultation showed a few mucous râles distributed over both lungs, most numerous in the inferior portions. The apex-impulse of the heart could be seen just outside the nipple line at the fifth interspace. There was systolic retraction in the third and fourth left interspace. A distinct presystolic thrill could be felt to the left of the sternum with a distinct shock following the impulse of the heart. The heart dulness extended on the left 17 cm. from the midsternum, to the second left rib above and 3 cm. to the right of the sternum. A loud, rough, presystolic murmur and a rather soft blowing systolic murmur were heard in the mitral area. The systolic murmur was transmitted to the left axilla and scapula. The pulmonary second was accentuated. The radial pulse was rapid and weak. The abdomen was much distended. The liver was not palpable but marked tenderness existed below the right costal edge. The spleen was not palpable. Free fluid existed in the peritoneal cavity. There was marked edema in the lower extremities, of the external genitals and also of the lower abdominal wall. Blood cultures made on March 25 and again on April 7 were negative. On April 1, 1200 c.c. of serous fluid were withdrawn from the peritoneal cavity; it contained a preponderance of polynuclear leucocytes and was sterile. On admission the blood examination showed, red cells, 4,600,000; hemoglobin, 72 per cent.; leucocytes, 11,600.

Course of Disease.—On April 7 the leucocytes were 10,400. The urine was scant and remained so throughout the patient's stay in the hospital. In the many specimens examined there was a trace of albumin, a few hyalin and granular casts and occasionally a few red cells. The patient's temperature was of an irregular septic type ranging from normal to 103 but usually was from 99 to 100.5 in the morning and from 100 to 104.6 in the afternoon. Gradually the patient failed and died on April 13, 1904. The autopsy, made five hours after death, revealed:

Anatomical Diagnosis.—Stenosis of the mitral orifice; acute vegetative aortic endocarditis; cardiac hypertrophy and dilatation; localized fibrinous pericarditis; bilateral serofibrinous pleuritis; recent hemorrhagic infarct in upper lobe of right lung; pulmonary edema; hydroperitoneum; anasarca; passive hyperemia of liver, kidneys and spleen.

Blood cultures made from the heart's blood and vegetations on the aortic valves showed the presence of a streptococcus.

CASE 5.—S. N., male, single, aged 21, was admitted to the presbyterian Hospital, Chicago, April 23, 1907; died July 17, 1907. Diagnosis: infective endocarditis, pneumonia, mycotic aneurism and aortic insufficiency.

History.—On admission the patient stated that he had been well until three years ago. At that time he suffered from an acute polyparthitis with fever. He was not able to walk for two or three months. Following this he suffered from palpitation of the heart and shortness of breath upon exertion. At times there was pain in the region of the heart. Five months before admission the patient suffered from severe headache, general weakness and poor appetite. There was shortness of breath on exertion and he suffered from throbbing and rapid action of the heart. A month later, with the continuation of the symptoms, there occurred a dull pain in the palm of the left hand. This shifted soon to the left hip and soon afterward disappeared. About a month before admission the patient again suffered from pain in the left hip, knee and ankle and was treated for sciatica by a physician. Two weeks before admission this pain in the left hip became very severe and the sharpest pain was located just above the left hip joint and became constant. Since that time the pain had increased, had been throbbing in character and the hip had been very tender. During the last five months the patient had lost thirty pounds in weight.

Examination.—The patient lay on the right side; was very restless and appeared to be in great pain. His face was pale with a little cyanosis of the lips, finger-nails and visible mucous membranes. When he attempted to walk the pain in the left gluteal region was increased. The throat was normal. The lungs showed nothing abnormal. The apex-beat of the heart was in the fifth interspace just inside the mammillary line. There was no thrill. The left border of heart dulness extended 1 cm. to the left of the left nipple and the right border was on the right sternal edge; the upper border at the third left rib. There is a soft diastolic murmur of low pitch heard best over the aortic area and transmitted down the sternum. The pulse was water-hammer in character and there was a capillary pulsation of the fingers and of the lips. The liver was palpable, soft and normal. The spleen was palpable, firm and moderately tender. The left gluteal region was swollen, elastic and very tender. There was a distinct pulsation synchronous with the heart action. A distinct thrill was obtained on pressure over the swelling and a distinct bruit was heard on auscultation. The pulse of the popliteal arteries was equal. The blood showed 4,300,000 red cells, 70 per cent. hemoglobin and 6,900 leucocytes.

Course of Disease.—On April 30 the leucocytes were 13,600; on May 16, 14,300 and gradually increased to about 23,000 on May 25, then declined in number and on June 25 were 10,000. The hemoglobin gradually fell to 50 per cent. on June 25 and the red cells to 3,300,000 on the same date. The urine was loaded with amorphous urates; specific gravity, 1.029; it contained a trace of albumin with a few hyalin and granular casts. Toward the end of the illness a few red cells were found in the urine. On April 30 blood culture revealed the pneumococcus in pure culture; again the same result on May 5. The temperature curve was distinctly septic as shown by the chart. On May 12 a needle was introduced into the aneurismal swelling of the gluteal region and pure bright blood was obtained

at the depth of 3 cm. From this blood a pure culture of the pneumococcus was obtained. On June 16 a small pulsating mass was developed under the left jaw and grew in the last few days to the size of a walnut. It was distinctly pulsating and showed a thrill on pulsation and a bruit on auscultation. On June 24 a petechial rash appeared on the skin and conjunctiva. On June 19 in the afternoon there suddenly developed a complete right-sided hemiplegia and the patient passed into coma and died.

Beginning on May 14 the patient was vaccinated with his own dead pneumococci. This was repeated on May 23, June 1 and 10. The result of these vaccinations on the clinical course, the blood and the autogenous bacteria was practically the same as in other patients. (See Chart 3.)

Case 6.—Miss E. T., aged 18, schoolgirl, was referred to my consultation room by Dr. C. M. Johnson, of Harvard, Ill.; died Sept. 1, 1908. Diagnosis: infective endocarditis, pneumococcemia and mitral insufficiency.

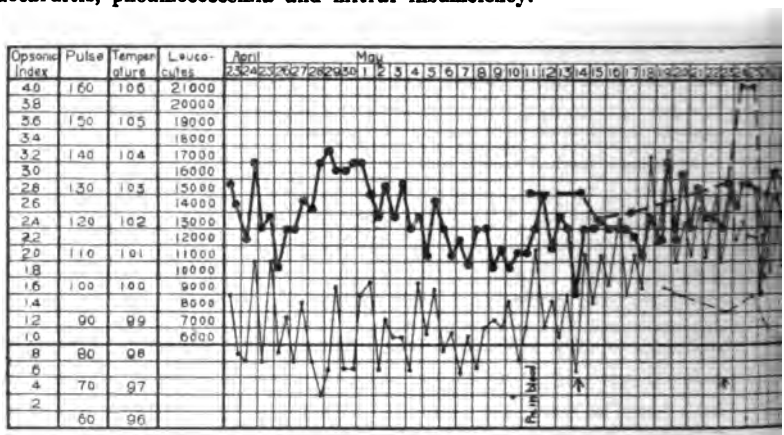
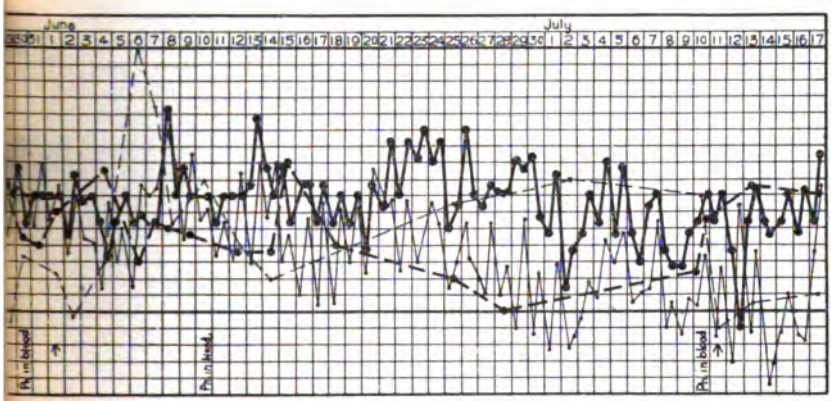


Chart 3.—Pulse, temperature, leucocyte and pneumococco-opsonic index curve heavy line, leucocytes; broken fine line, pneumococco-opsonic index. Injections

History.—The patient came to Chicago with her mother, after traveling for two hours on a railway. The history given was that she always had been delicate and had suffered from all of the ordinary diseases of childhood. The catamenia were established at 14 years and were of the twenty-eight-day type. From the time she was 12 to 13 years of age the patient suffered from epistaxis, which persisted until the nasopharynx was treated by a specialist. She was a student in the University of Illinois during 1907 and worked hard. During the winter of 1907-8 she suffered from an attack of acute tonsillitis and was in bed for one week. Following this illness she attended to her duties and returned to her home in June. At that time she recognized that she was weak, had no endurance, was very nervous, had no appetite, poor sleep, dyspnea on exertion and suffered from palpitation of the heart.

Examination.—When seen on July 14, 1908, the patient was pale, general nutrition poor, general muscular weakness manifested by tremulousness. The tonsils were only moderately enlarged and were not red or visibly infected. The left border of the heart extended 11 cm. from the center of the sternum; the base to the left second rib and the right border to the right sternal edge. The apex-beat was diffuse and the heart action tumultuous. Loud systolic and diastolic murmurs were heard over the whole precordia. A very loud rough systolic murmur was heard in the mitral area transmitted to the left axilla and back. The pulmonary second tone was moderately accentuated. With the exception of a few moist râles over the bases, there was nothing abnormal to be found in the lungs. The liver was palpable at the costal edge. The spleen was palpably enlarged and not tender. The abdomen was contracted. There were no purpuric spots discernable. The blood showed 3,500,000 red cells, 50 per cent. hemoglobin, 21,000 leucocytes. A blood culture made at this time showed 6,500 colonies of the pneu-



in Case 5. Solid heavy line indicates pulse; solid fine line, temperature; broken dead organisms indicated by arrows.

mococcus in pure culture from each cubic centimeter of blood. The urine showed a trace of albumin without other abnormal elements. The temperature was 101.6, the respirations 30 and the radial pulse 140 per minute.

Course of Disease.—The patient was sent to her home with a letter to the physician indicating the diagnosis and treatment. She declined steadily. Two vaccinations of the autogenous pneumococcus were made on Aug. 7, 1908, and about one week later. Following the first dose of vaccine (200,000,000 dead pneumococci) there was less fever and the patient appeared brighter for two or three days. The second vaccination produced no apparent effect. On August 26 there were three subcutaneous nodules which were small, slightly red and tender. No petechial spots appeared. The patient died Sept. 1, 1908, and no autopsy was obtained.

CASE 7.—Miss S., aged 21, student, seen with family physician, Dr. George Keenan at Madison, Wis., June 2, 1907; died in July, 1907. Autopsy. Diagnosis: chronic infective endocarditis, pneumococcemia and pulmonary vegetative valvulitis.

History.—The patient had always enjoyed good health until the beginning of the present illness, about fourteen months ago. During the latter part of the preceding year she was a student in the university and became nervous, languid, had a poor appetite and was obliged to give up her studies. During the summer vacation there was some improvement in the general condition, but no record was made of any physical examination during that time. She had not suffered from any local infectious disease like tonsillitis. During the fall of 1906 she attempted school work again but soon was obliged to give it up because of lessened strength and endurance, poor appetite, general nervousness and dyspnea on exertion. It was noticed that she was pale and there was a slight cough, especially on exertion, which was believed to be due to a cold. During that time it was noted that the temperature ranged between 99 in the morning to 102 in the evening. A tentative diagnosis of probable tuberculosis was made and the patient was sent south for the winter. There she was out of doors and made some general improvement but remained weak, had a poor appetite, shortness of breath on exertion and had more or less cough, especially after exertion or immediately after changing from a sitting to a standing position or immediately after lying down. She returned to her home in the early summer and remained up and about.

Examination.—The family physician finally was called and found an evening temperature of 103, a rapid pulse, a secondary anemia with 3,624,000 red cells, 6,500 leucocytes and 55 per cent. hemoglobin. The urine was normal. A consultation was held at this time with Dr. Ogden, of Milwaukee, and resulted in the finding of a few crackling râles over the top of the right lung, palpable splenic enlargement, secondary anemia, a blowing murmur over the base of the heart with rapid heart action and much physical prostration. The temperature from that time was intermittent in character; normal or nearly so in the morning with a rise to 102 or 103 or more in the evening. (See Chart 3.) On June 2, 1907, when seen with Dr. Keenan, the general physical condition as mentioned above was noted but more particularly there was a rapid and tumultuous heart action, together with murmurs during both phases of the heart action and heard over the whole precordia. No petechial spots could be found on the skin or mucous membranes. The spleen was enlarged and somewhat tender. A few crackling râles could be heard over the bases of both lungs posteriorly. There was no consolidation. The abdomen was moderately distended; the liver palpable and moderately tender. The pelvis, examined per rectum, showed a normal condition. A specimen of blood showed a tuberculo-opsonic index of 0.7; a pneumococcus opsonic index of 0.6 and a streptococcus opsonic index of 0.7. Blood cultures were made by Dr. E. C. Rosenow, and the pneumococcus in pure culture was obtained.

Course of Disease.—Following this diagnosis the progress of the case was rather rapid and death followed early in July, 1907. In the interval between June 10 and the death of the patient she was inoculated with the autogenous dead pneumococcus in small quantities; not more than 2,500,000 to 5,000,000 of the bacteria were used. Following the vaccinations there was some improvement

in the clinical phenomena as evinced by a lessened height of the evening temperature and the patient said that she felt better. (See Chart 4). The pulse-rate and the physical signs did not change. Four days before death a moderate pulmonary hemorrhage occurred and the patient failed rapidly and died from exhaustion. An autopsy was made.

Anatomical Diagnosis.—Vegetative and ulcerative endocarditis of the pulmonary valves and arteries; subcutaneous and renal hemorrhages; multiple old and recent pulmonary infarcts; serofibrinous pleuritis; cloudy swelling of the heart, liver and spleen; hyperplastic splenitis; anemia; passive hyperemia of liver and spleen; hydrothorax; hydroperitoneum and hydropericardium.

Postmortem Examination.—It was noticed particularly that the pulmonary valves were covered with large grayish-yellow cauliflower-like vegetations which nearly filled the lumen of the arteries at the base of which the valves were ulcerated. Some of the masses were 2 cm. long. The intima of the pulmonary arteries just above the valve was ulcerated. At the point of the bifurcation of the pul-

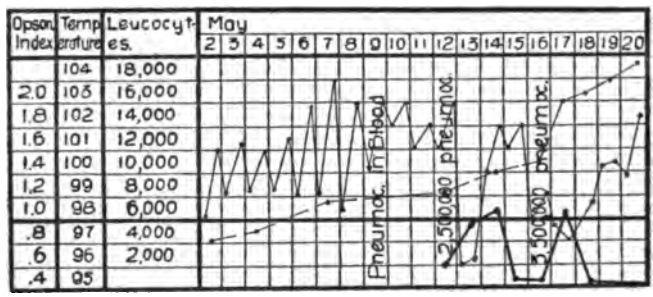


Chart 4.—Pneumococco-opsonic index, temperature and leucocyte curves in Case 7. Solid heavy line indicates pneumococco-opsonic index; solid fine line, temperature; broken fine line, leucocytes. (From the *Journal of Infectious Diseases*, Chicago.)

monary arteries there was a thrombus which was 0.75 cm. thick, solidly attached and could be followed to the left upper lobe where it ended in a softened infarct. Several small branches of the left pulmonary arteries were thrombosed. In the right lung was also an extensive thrombosis, in a branch which led to the left infarct in the lower lobe. After removal of some of the thrombi from the smaller branches the intima appeared rough and even ulcerated.

Bacteriologic Examination.—A pure culture of the *Streptococcus pyogenes* was obtained from the fluid in the peritoneum, pleural and precordial sac and from the heart's blood as well as from the spleen, liver, heart and the large infarctions. The *Staphylococcus aureus* was also found in softened infarcts. Emulsions from the vegetations on the tricuspid valve and ventricle contained both streptococci and pneumococci, of which the former were the more numerous.

CASE 8.—Mrs. N. W., aged 35, first seen as ambulatory patient, Dec. 18, 1907; confined to bed at last account: Diagnosis: chronic infective endocarditis, pneumococcemia, mitral stenosis and cardiac dilatation.

History.—The patient had borne three children; she had been fairly well until a year ago before she came under observation. There was no history of rheumatic fever or any other acute infectious disorder. During the last year she had been treated for various complaints including possible pulmonary tuberculosis and because of the latter diagnosis had lived much in the open air and had attempted to exercise, even when this caused great discomfort. When first seen the patient complained of shortness of breath on exertion, general weakness, some edema of the ankles and during the day an inability to lie flat in bed or on the right side, a sense of fulness and of oppression in the chest which amounted to pain on the slightest exertion. These symptoms began a year before admission and gradually increased to the maximum at the present time.

Examination.—This showed marked pallor with cyanosis of the lips, visible mucous membranes and finger-nails. The mucous membrane of the mouth and throat was pale and there was no evidence of infection about the teeth or throat. The lungs showed a few moist and dry râles over both apices and at the bases. There was no evidence of consolidation anywhere in the lung. The left border of the heart was 15 cm. from the midsternum, the apex at the sixth interspace. There was a marked thrill at the apex. A rough presystolic murmur was heard in the mitral area and there was a very marked accentuation of the second pulmonary tone. The left auricle was much dilated. The right border of heart dulness extended 2 cm. to the right of the sternum. There was no venous pulse in the neck. The abdomen was moderately distended. The spleen was not palpable. The liver could easily be palpated and was tender to the touch.

Course of Disease.—The patient was sent to the Presbyterian Hospital, where subsequent examinations confirmed the findings made above. The urine examined on several occasions showed a trace of albumin, with a few hyalin and granular casts. The temperature for nearly two months while the patient remained in the hospital was usually normal in the morning and from 100 to 101 in the afternoon. A blood culture made on May 5, 1908, gave a pure culture of the pneumococcus. Immediately after this the patient returned to her home in Iowa, where she was under the care of a local physician who was directed to keep the patient in bed under hygienic surroundings and to attempt to improve the resistance of the patient by supporting treatment. On Sept. 10, 1908, an inquiry was made by letter and the statement came back from the husband of the patient that she was not as well, was very weak and confined to her bed with a low form of fever. The pneumococcus obtained by culture resembled that obtained from other patients suffering from a like condition. A subculture of this organism was injected into the vein of the ear of a rabbit and produced vegetative aortic endocarditis from which the animal died.

CASE 9.—Mr. E. H. B., aged 29, single, clerk, was seen in consultation with Dr. Blatchford, of Chicago, in July, 1905; died in November, 1905. Autopsy: Diagnosis: chronic infective endocarditis, streptococcemia, aortic insufficiency and mitral insufficiency.

History.—The patient had always been a vigorous, healthy man who had suffered from no important disease in his life. On April 10, 1905, he had a moderately severe attack of tonsillitis which confined him to his bed for three days. He then returned to work and appeared to be in the usual condition of health until

the latter part of June, 1905. He then noticed lessened strength and endurance and was nervous and irritable. On July 24, 1905, his physician found him with a high fever and general prostration.

Examination.—On July 25 the physician found the patient's temperature 101 F., pulse 90, respiration not accelerated. The only abnormal physical finding was some swelling of the left knee-joint with moderate tenderness and no redness. The first tone in the mitral area appeared to be somewhat impure. The hemoglobin was 95 per cent., red cells 4,900,000 and leucocytes 16,000. The differential count of the leucocytes showed a normal condition. On Aug. 1, 1905, Dr. E. C. Rosenow made a blood culture and isolated an organism which appeared to be a streptococcus in pure culture. When inoculated in large doses into animals the organism appeared to be of a low grade of virulence.

Course of Disease.—On August 2 an aortic systolic murmur was heard and the left border of dulness extended 10 cm. to the left of the midsternum. On August 4 there was pain and swelling of the left ankle lasting for a few hours. On August 20 there was a slight swelling and tenderness of the right wrist. On Sept. 5, 1905, there was severe abdominal pain lasting for twelve hours, the cause of which was not clear. During August and September the leucocyte count varied between 14,000 and 25,000 with a normal proportion of the various white cell elements. During August a diastolic aortic murmur developed and later a mitral systolic murmur was heard. The temperature was of a septic type about 99 in the forenoon and varying from 100 to 104 in the evening. About every six to eight days there was usually a sudden elevation of temperature without chill which was accompanied by an increased leucocytosis. Petechial spots appeared a short time before death in the latter part of November, 1905. During the latter part of the illness there was dilatation of both sides of the heart with a loud systolic murmur, heard in the mitral area and transmitted to the left and a soft blowing diastolic murmur in the aortic area transmitted down the sternum. The spleen was palpable and tender, the liver slightly enlarged and tender, and the urine contained a trace of albumin, a few hyalin and granular casts and a few red cells. An autopsy was held.

Anatomical Diagnosis.—Acute vegetative and ulcerative endocarditis of the aortic and mitral valves with aneurism of the aortic valve and beginning dissecting aneurism of the aorta; hypertrophy and dilatation of the heart; ecchymosis of pericardium; fatty degeneration of myocardium; hydropericardium; hydrothorax; hydroperitoneum; passive congestion of liver and spleen; acute nephritis; old and recent renal infarcts with deformity of right kidney; periappendiceal adhesions.

Bacteriologic Examination.—Cultures from the heart valve showed the streptococcus alone. Cultures from the kidney were sterile. The organism found in the cultures from this patient's blood and from the vegetations on the heart valve was called the streptococcus. As stated above, it was of low virulence, for when injected into animals in large amount it did not cause death. At this time subcultures of the organism were not studied by Dr. E. C. Rosenow as was done in subsequent cases. This so-called streptococcus grew in plate cultures and showed the lessened virulence of strains of organisms obtained from other patients when given in subcultures, injections of which into animals was followed by recovery

and which proved to be the pneumococcus. In all probability therefore, the organism found here was the pneumococcus but is presented in this group of cases of the streptococcus. The vegetations on the valves grew in a dense mass as in other cases of pneumococcemia and endocarditis.

This patient had been repeatedly treated with injections of a commercial antistreptococcal serum without benefit.

CASE 10.—Mr. J., aged 52, lumberman, was seen with his physicians, Dr. McKechnie and Dr. J. L. Miller, of Chicago, in November, 1908; died March 4, 1909. Autopsy. Diagnosis: infective endocarditis, pneumococcemia, mitral insufficiency.

History.—The patient had been a strong and healthy man all his life. His business cares were great. He was addicted to tobacco and the overuse of alcohol. No history of venereal disease could be obtained. Off and on for several years he had suffered from various muscular ailments and disturbances of the digestive organs due to habits of life but had never presented any evidences of physical disease of importance. During the summer of 1908 the patient suffered from abscesses about the gums with pyorrhea alveolaris. This had noticeably infected the right upper second bicuspid tooth and an abscess developed also over the left upper first molar for which he received treatment from his family dentist. During the late summer of 1908 the gums and teeth were in bad condition, many of them loose. In July, 1908, the patient noticed a lessened strength and endurance; at times was chilly and when the temperature was taken on a few occasions it was found to range as high as 100. No record of the temperature was kept at this time and the feeling of ill health was supposed to be due to overwork. At this time it was noticed, too, that he had transient attacks of pain and some swelling in the various joints, especially of the feet, which appeared to be definite rheumatism. In the early part of November he was on a hunting and fishing trip and returned home in a worse condition than before his vacation. His physician found on examination no special physical disturbances except slight swelling and tenderness in the right great toe-joint. This was diagnosed as gout. The patient remained at home from this time on, with a gradual loss of strength and temperature ranging from 98 to 99 in the morning to 100 to 102.5 in the evening. In the latter part of November, 1908, a blood examination showed 11,000 leucocytes. To determine the cause of the temperature a Widal test was made at the Municipal Laboratory of Chicago and was said to be positive. The patient was then placed on typhoid orders and treated as a typhoid fever patient for two or three weeks. He then suffered from a sudden left-sided hemiplegia with a rapid rise of temperature to 106. The temperature soon dropped to the former range; the hemiplegia improved and the patient returned to much the same condition as before. The examination of the heart up to this time had been entirely negative. From this time onward a systolic murmur was heard occasionally and later became permanent. The left heart border was extended to the left and the pulmonic second tone was somewhat accentuated.

Examination.—Early in December I saw the patient with his physicians and confirmed the physical findings noted by them; that is, a septic type of temperature; a slight left hemiparesis; the patient conscious but answering questions slowly and taking but little interest in his surroundings; slight dilatation of the

left heart with a mitral systolic murmur transmitted to the left and accentuation of the second pulmonic tone; the lungs negative; the liver palpable, enlarged and somewhat tender; the spleen not palpable; a few petechial spots in the skin in various parts of the trunk and extremities. Blood cultures were made by Dr. E. C. Rosenow on December 6, 1908. The first two blood cultures were negative but a third and a fourth culture yielded the pneumococcus. Repeated Widal tests now proved to be negative. On December 13 the hemoglobin was 85 per cent., the red cells 4,000,000, the leucocytes 17,700 with a preponderance of polymorphonuclears. On February 22, 1909, hemoglobin was 70 per cent., red cells 3,200,000, leucocytes 12,000.

Course of Disease.—The patient was vaccinated with his own dead bacteria on several occasions without any manifest signs of improvement. He was also given intravenous injections of normal human serum which were followed by a marked reaction consisting in a rise of temperature, rapid heart action, etc. The details of the results of these vaccinations and of the use of human serum will be discussed in a paper by Dr. E. C. Rosenow. The patient continued in this condition until March 4, 1909, when he died from exhaustion.

Unfortunately an undertaker had embalmed the body before consent was given for an autopsy.

Autopsy.—This showed a markedly hypertrophied and dilated heart, vegetative and ulcerative endocarditis of the mitral valves, infarcts of the kidneys and spleen and fatty degeneration of the liver. Large massive vegetations were found on the mitral valve. These were grayish-red. Both anterior and posterior leaflets were involved. The growths were situated on the upper surface of the valves and extended for a distance of 2 cm. into the auricle. The free margin of the masses of vegetations were necrotic.

CASE 11.—T. W., male, single, aged 35, was admitted to the Presbyterian Hospital, Chicago, Oct. 7, 1905; died Nov. 17, 1905. Diagnosis: infective endocarditis, streptococcemia and mitral insufficiency.

Present Illness.—The patient came to the hospital complaining of pain, weakness and lassitude; shortness of breath on exertion; lessened appetite and poor sleep. He gave no history of previous illness of importance and a negative family inheritance.

Physical Examination.—This showed slight blueness of the lips and visible mucous membranes and general pallor; throat normal. Lungs showed no evidence of physical change; left border of heart dulness extends beyond the nipple line, the base to the third rib and the right border to the right edge of the sternum. A rather loud systolic murmur replaced the first sound of the heart and was transmitted to the left. The arterial walls appeared to be thickened. The abdominal organs were negative. The blood pressure taken with a Stanton instrument was 155 mm.

Course of Disease.—On October 9 a few moist râles were heard at the bases of both lungs. There was cough with slight mucopurulent sputa which was negative for tubercle bacilli. A blood culture was attempted on October 17 and was negative. The urine on admission and during October showed diminished amount for twenty-four hours with a specific gravity ranging from 1.010 to 1.020,

albumin usually absent. A few hyaline and granular casts usually present and a few shadows of red cells were usually found. On October 25 a blood culture was made and a streptococcus-like organism in pure culture was obtained. On October 27 the spleen was palpable for the first time and petechial spots were noticed in the skin of the chest and abdomen. From this time onward petechial spots occurred in crops. On November 6 a second positive blood culture with the streptococcus was obtained. The urine contained at this time a few red cells and a few white cells with a trace of albumin and a few hyalin and granular casts. On November 6 a blood examination showed 3,600,000 red cells, 16,450 leucocytes and 61 per cent. hemoglobin. The temperature of the patient during the stay in the hospital was of septic type ranging in the morning about 99 and from 101 to 102 and on a few occasions as high as 103 to 103.8 in the evening. The pulse-rate was rapid, ranging from 100 to 120; respirations from 24 to 36. On November 14 the patient received 20 c.c. of antistreptococcus serum and this was repeated on November 15. There was no alteration in the clinical symptoms after the use of the serum and the patient died of exhaustion on November 17. No autopsy was obtained.

The organism isolated in this case, like that in Case 9, was not studied as carefully as the organism from later cases, but it had the morphologic characteristics of the organism which later also proved to be the pneumococcus. It is, however, classed as a streptococcus infection in this series.

CASE 12.—W. P., aged 35, male, manufacturer, was seen in consultation with Dr. H. B. Favill, of Chicago, in October, 1903; died. No autopsy. Diagnosis: infective endocarditis, pneumococcemia, aortic insufficiency and mitral insufficiency.

History.—During childhood patient suffered from severe attacks of rheumatic fever in which the endocardium was involved. As a result he suffered during childhood and thereafter from a mitral insufficiency which became fully compensated and caused him no especial inconvenience excepting that with continued overexertion he suffered from a moderate dyspnea and palpitation of the heart. In the fall of 1902 the patient suffered from a low type of fever which was pronounced typhoid by the physicians in charge. The patient was confined to his bed or house for over two months and had a slow convalescence. There was doubt expressed by the physician who was in consultation at the time that this was typhoid, but in the absence of definite signs of any other disease, the patient was treated for typhoid fever. Following this attack the patient did not regain his usual strength and vigor. He appeared pale, listless and expressed himself as feeling weak and tired. He remained for a time at Hot Springs, Va., taking the baths, from which he received no benefit. During the early fall of 1903 he again was confined to his house and bed with a low form of fever which proved to be septic in character. He suffered from dyspnea especially on the least exertion, cough, rapid heart action and great nervous irritability. The heart was moderately dilated to the left and there was a loud rough systolic murmur heard in the mitral area which was transmitted to the left, and a soft blowing murmur in the aortic region transmitted down the sternum.

Course of Illness.—The spleen became palpable, the urine contained microscopic blood with a trace of albumin and a few hyalin and granular casts.

Petechial spots later appeared in the skin in successive crops. When the patient was seen in consultation with his physician, Dr. Favill, a blood culture was suggested which was made and proved to be a pure culture of the pneumococcus. This was verified by subsequent cultures and by subcultures and by injections into animals. The patient died of exhaustion and no autopsy was permitted.

In the light of the termination of this case, it is not improbable that there was a low grade of infective endocarditis during the time it was diagnosed as typhoid fever and in the interval between that and the final illness there was a continuation of the heart infection which finally became so severe that the patient became bedridden.

CASE 13.—Miss F. S., aged 18, was admitted to the Presbyterian Hospital Oct. 28, 1907, on the service of Dr. B. W. Sippy, who requested me to see the patient with him and has kindly consented to a report of the patient in this series. She died Jan. 22, 1907. Autopsy. Diagnosis: Infective endocarditis, pneumococcemia, aortic and mitral insufficiency.

History.—Patient had an attack of acute rheumatic fever six years before admission which left a mitral lesion. Three months before admission to the hospital she had an attack of pain in the right side of the chest of a sharp, sticking character which was aggravated by breathing and by coughing. There was some fever but no cough. The patient remained in bed for a week and then got about but did not feel well and it was noted that there was usually an evening temperature varying from 100 to 101 or more. She felt weak for a long time, had a poor appetite and was nervous and irritable. Three weeks before admission the left ankle became swollen and painful. This lasted for a week. No other joint involvement occurred. On admission the patient complained of chilliness, followed by a sensation of heat, prostration and weakness. The bowels were regular, the appetite good. The patient slept fairly well.

Examination.—On admission there was a decided pallor of skin and mucous membranes. There were no petechial spots; no enlargement of the superficial lymphatic glands. The patient was fairly well nourished. There was no infection of the throat. The lungs were normal. Cardiac dulness extended to the left outside of the mammillary line. There was no evidence of dilatation of the right heart. There was a presystolic and systolic murmur in the mitral region and the systolic murmur was transmitted to the left. The pulse was rapid but regular. The spleen was not palpable.

Course of Disease.—On November 4 for the first time there was heard a diastolic murmur in the aortic area which was transmitted downward and a water-hammer pulse and capillary pulsation were noted. On November 18 the spleen was distinctly palpable. On November 25 there was pain in the left side of the chest and in the shoulder, aggravated by breathing. On December 2 the patient complained of a severe pain in the left hypochondrium and the spleen was tender. There was a secondary anemia, hemoglobin diminished to 50 per cent. and a moderate leucocytosis with a normal proportion of white cells. The coagulation time of the blood was 3.5 minutes. On December 25 the patient suffered from an acute attack of pneumococcus tonsillitis. The submaxillary glands were tender and swollen but did not suppurate. Petechial hemorrhages of the skin appeared for the first time. The pneumococcus in pure culture was obtained from the blood.

From this time on the patient failed rapidly. The pneumococco-opsonic index was below the normal and the leucocytosis increased. There was a progressive secondary anemia with hemoglobin reduced to 28 per cent. The pulse remained regular until a short time before death, when the heart became dilated and irregular in action.

An autopsy was held on January 22 and revealed:

Anatomical Diagnosis.—Ulcerated mitral, aortic and mural endocarditis with characteristic vegetative growths. There were multiple infarcts of the spleen; petechial hemorrhages of the skin; anemia; fibrinous pleuritis and peritonitis; acute tracheobronchial lymphadenitis; hyperplasia of the spleen; edema of the lungs; cloudy swelling of the liver, kidneys and myocardium; hypertrophy and dilatation of the heart; obliterative fibrinous pericarditis.

Bacteriologic Examination.—From the serum, blood, peritoneal fluid, right pleural exudate and from the emulsion of the vegetation of the heart valves there were obtained Gram-positive cocci arranged in clusters and chains and in twos and from the vegetations emulsion there was obtained also a Gram-negative bacillus. Seven cultures gave a proportionately large number of pneumococci, a few *Staphylococci aurei*, and the blood yielded the *Streptococcus pyogenes* in addition. The *Bacillus mucosus* also was obtained from the vegetation emulsion.

The characteristics of the pneumococcus obtained from the blood before and after death were exactly similar to those described in the earlier part of the paper.

This patient was inoculated with the dead pneumococci of her own culture. Chart 5 shows the dates of inoculation, the dose and the result upon the temperature, the leucocytosis and the pneumococco-opsonic index.

CASE 14.—A. K., male, married, aged 30, was seen with his family physician, Dr. Frank S. Johnson, Chicago; condition practically unchanged at last account. Diagnosis; infective endocarditis, pneumococcemia, mitral insufficiency and aortic insufficiency.

History.—During childhood the patient suffered from acute rheumatic fever with a sequel of mitral insufficiency and aortic insufficiency. Compensation occurred and the patient did not suffer in consequence until his twentieth year. During his freshman year (1897-98) in college he attempted athletic work in rowing, track running, etc., with the result that during the holiday season he was confined to his bed with broken heart compensation. After a long rest compensatory hypertrophy was restored and the patient remained in fair condition of health until the early part of 1909. At this time he noticed a lessened strength and endurance, a good deal of nervousness and irritability, slight shortness of breath on exertion with some palpitation of the heart and a subfebrile temperature was noticed. He went to Hot Springs, Va., to rest and recuperate and while there became worse. Chills followed by fever occurred at irregular intervals. The spleen became palpable and he grew pale, weaker, had great dyspnea and palpitation of the heart. On the patient's return to Chicago a septic type of temperature continued, with an occasional chill, increasing weakness, palpitation, shortness of breath, etc. A secondary anemia with a low white blood count was found and his physician discovered pigmented parasite-like bodies in the red

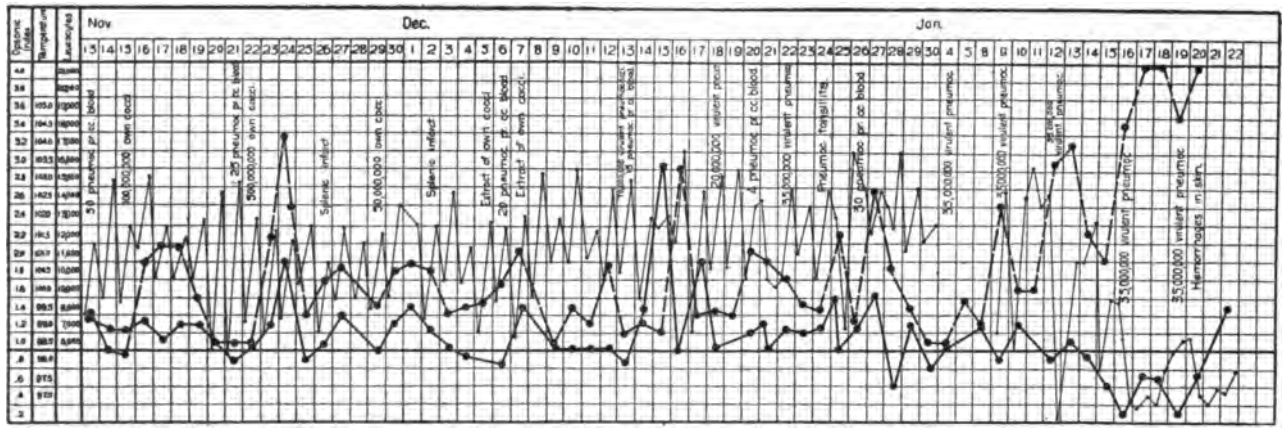


Chart 5.—Pneumococco-opsonic index, temperature and leucocyte curves in Case 13. Solid heavy line indicates pneumococco-opsonic index; solid fine line, temperature; broken heavy line, leucocytes. (From the *Journal of Infectious Diseases*, Chicago.)

corpuscles. Antimalarial treatment was given with some amelioration of symptoms but a continuation of the febrile condition, the weakness, etc.

Examination.—When seen in consultation on May 25, 1909, the patient was found to be pale and weak; a few petechial spots were found in the skin of the back, the heart was dilated especially to the left and the heart action was rapid. A soft blowing diastolic murmur was heard in the aortic area and transmitted down the sternum, also a loud systolic murmur in the mitral area transmitted to the left with accentuation of the second pulmonic tone. The lungs were clear. The spleen was palpable; the liver not enlarged; the urine practically normal.

Immediately thereafter two blood cultures were made which were negative. On May 29 and June 10 blood cultures were made by Dr. E. C. Rosenow and a pneumococcus in pure culture was isolated both times. This organism proved to have all the characteristics of the pneumococcus isolated in other cases of infective endocarditis.

The patient died in July. Autopsy revealed vegetative growths on aortic and mitral valves; aortic and mitral insufficiency; infarcts of spleen and kidneys, etc.

100 State Street.

ABSTRACT OF DISCUSSION.

DR. ALFRED STENGEL, Philadelphia: Dr. Billings has opened up a subject of great practical importance, particularly from the point of view of the recognition of these cases, the diagnosis of the condition. While the proportion of cases, the acute cases, in Dr. Billing's series is rather large, it will be admitted I think that, as a rule, these cases are secondary, that is, secondary to an old endocarditis. I think the disproportion is very great, probably 8 out of 10, or 9 out of 10, and cases of this type are really engrafted on an old lesion.

The interpretation of the development of fever in those cases mistaken for tuberculosis in patients with an old endocardial lesion is an interesting question, and a very important question for the practitioner. This is a problem that comes to us time and time again. Among the other things to think of is the possibility of the development of such a lesion as this which the Germans call "efflorescing or recurring" endocarditis. There are causes of elevated temperature in old cardiac cases besides this; it would be a pity if we were misled into believing that this is the only cause of long-continued fever in people with old valvular lesions. Among other things, this fever will be found in old people, especially in cases of long-continued congestion in which there is a one-third broken compensation. In the aged, pyelitis or cystitis might cause a rise in temperature which might easily be mistaken for this. There should be a direct recognition of these cases. I have been looking over my records of the cases that have come under my observation (and these records are reasonably complete), and in fifteen of them I was struck with the peculiar frequency of marked anemia. Most of the patients, or many of them, developed marked anemia which resembled very much pernicious anemia. There was a low blood count and a rapid exhaustion or using up of the hemoglobin. The disproportion was more of the chloranemic type. There was also leucocytosis.

Again, the patient may present evidences of altered metabolism; albuminuria may develop as a result of lesions in the kidney, and the patient may suffer from

the presence of a small embolus in the spleen. Sometimes there may be rashes in the skin as after a pneumococcus or streptococcus infection, a type of rash that occurs in erythema multiforme.

In my cases the great majority have been streptococcic; that is, bacteriologists reported them as being streptococcic in type. In one case, however, an anaerobic bacillus was found. In another case it was reported that the bacillus of Welch was found, but without any definite certainty. I have no doubt but that Dr. Billings is correct in his statement that the organisms accustom themselves to their environment and so become of lesser virulence. I have had a young girl in the hospital who for five months has had streptococci in the blood. Possibly they are the older pneumonic bacillus Dr. Billings speaks of. The conditions found would be impossible in a streptococcemia of another source. The organism here accustoms itself to the patient and the patient accustoms herself to the organism and she lives on. In one case streptococci were found in the blood and were found from time to time throughout one entire year. In another case the duration of the illness was over eighteen months and for various reasons the organism was in the blood during this entire period. So there is a possibility in long-continued infections of an organism of reduced virulence being present in the blood.

Dr. DeLancey Rochester, Buffalo: In the last year I have had four cases of chronic lung disease which gave all the symptoms and physical signs of pulmonary tuberculosis. In the sputum I persistently found pneumococci arranged in streptococcic forms; so much so that cultures were taken from the blood in two cases. In one case the organism was found in the blood culture. I cannot tell what medium was used, because the work was done by an assistant. The same organism described by Dr. Billings was found in one case. The other cultures were negative. I present this as bearing on the organisms in chronic cases of disease.

Dr. John A. Witherspoon, Nashville: In my section of the country we do not get pneumonic infections as they occur in Chicago. In the last few years three cases have interested me very much. They proved to be gonococcus endocardial infections. In one case there was rheumatic involvement of a joint and infection of the seminal vesicles, etc.; examination of the blood showed a gonococcus infection. This was a rapidly fatal case. No previous heart lesion had existed. The other two patients had prior endocardial trouble; the condition has assumed a recurring form now with slight rise of temperature. It seems to me that while the streptococcus is by far the most common as a causative factor, we should not forget that other organisms, like the gonococcus, may produce later endocardial troubles of this kind.

Dr. Walter L. Bierring, Iowa City, Iowa: One of the interesting features brought out in the discussion is the etiologic rôle of the pneumococcus in chronic infectious endocarditis, and in this connection I beg to refer to a few individual cases. I saw recently a man of 45, who had a chronic endocarditis affecting the mitral valve, accompanied by continuous fever, marked chloranemia and leucocytosis. Unfortunately, a blood culture could not be made. During the past year the patient had suffered an attack of pyorrhea alveolaris and a general infective process of the gums of four months duration, necessitating the sacrifice of fifteen teeth. Previous to this there was no other history of an infectious disease and the patient was not conscious of any heart trouble. During the past year I saw two cases of aortic stenosis in young persons, one a young woman of 19 and the

other a man of 27. The age precluded the thought of an arteriosclerotic origin for the valvular lesion, but in both there was no other history of infectious disease to be elicited except several attacks of suppurative tonsillitis or quinsy. Neither had any rheumatic fever. I am confident that infections of the throat and buccal cavity have an important bearing on the development of endocarditis, and the importance given to the etiologic rôle of the pneumococcus in the paper is suggestive, especially since it has its normal habitat in the buccal cavity where it leads a saprophytic existence, and in its pathogenesis is subject to much more variation than other infectious agents.

DR. JAMES M. ANDERS, Philadelphia: Dr. Billings' paper is to be commended because in the past chronic infectious endocarditis has been, as a rule, overlooked. I do not wish to underrate the importance of the pneumococcus as an etiologic factor in the disease, but in my experience the majority of these cases are secondary to an old sclerotic endocarditis of rheumatic origin. Even in these cases we may find streptococci in the blood. I agree with Dr. Stengel that cases which are secondary to chronic rheumatic or other forms of endocarditis offer some chance for recovery; they are by no means hopeless cases. In this connection it might be well to point out what measures of relief or even cure are available in cases of chronic infectious endocarditis. I think that whenever streptococci are found in the blood we are not only justified in using antistreptococcus serum, but we should strongly urge its use by others. There can be no doubt, from an examination of the literature, that in a number of cases remarkable recoveries have followed the use of this serum. I saw one case in which I believed that the chronic infective endocarditis was secondary to pulmonary tuberculosis. The possibility of the occurrence of chronic infectious endocarditis in the course of pulmonary tuberculosis is to be recollected. The diagnosis is naturally difficult in the extreme, but when there is marked tuberculosis of the lungs or other viscera, more particularly if a careful examination shows that no other form of infection exists, we are justified in making a reasonably certain diagnosis of infectious endocarditis of tuberculous nature.

Another point in the treatment of chronic infectious endocarditis is worthy of notice, namely, the open-air method. I cannot speak from personal observation, but I saw a case with another physician recently; this patient had been treated by the open-air method with excellent effect on the general condition.

So far as the treatment is concerned, we should bear in mind three points: First. Most cases occur among subjects who are more or less rheumatic. Second. Whenever streptococci are detected in the blood, even though other organisms are encountered in association, there should be used promptly the antistreptococcus serum. Third. The open-air treatment, as well as supportive measures, should be accorded a trial.

DR. CHARLES G. STOCKTON, Buffalo: Dr. Billings said very little about the prognosis and treatment of chronic infectious endocarditis, and I wish he would go a little more into detail as to his results in these cases and a little more into detail as to his conception of the treatment. It seems to me that his paper is important as bearing on a definite type of chronic infectious endocarditis which has undoubtedly gone long unrecognized. In the discussion, more than in the paper, there has been something said about differentiating the different forms of septic endocarditis; I do not understand what is meant exactly unless it is that the ordinary septic or malignant cases of endocarditis may be secondary to other focal lesions of the endocardium. A point of great practical importance, it seems

to me, is whether or not Dr. Billings got any benefit from the vaccines in the treatment of these cases of chronic infectious endocarditis.

DR. RICHARD C. CABOT, Boston: One year ago I heard Dr. Osler read the paper that has been referred to. Two points contained in it have since been verified in my own experience and I should like to allude to them. First. These people, or many of them, do not feel ill. One man after weeks of fever wanted to play golf. They often do not feel ill nor do they look ill. Second. A considerable number of these patients have tenderness of the "finger pads." This is a confirmatory minor point sometimes helpful in the diagnosis.

DR. FRANK BILLINGS, Chicago: I did not, as Dr. Stockton inferred, make any distinction in regard to the type of infection of the endocardium; both acute and chronic cases were engrafted on old endocardial lesions, as a rule, as every clinician has found. In my paper I referred rather to the type of fever. In acute infectious endocarditis due to the gonococcus, streptococcus, or what not, the temperature is not very high. One must not forget, in speaking of the physical signs in some of these cases, in mine, two out of fourteen, the lesion might be on the right side of the heart. In one the pulmonary valve was involved; in the other, the tricuspid. In one case emboli got to the lungs and caused a mistake in diagnosis; the physician in charge thought it was a case of tuberculosis. In regard to the prognosis, my experience with endocardial infections, whether acute or chronic, when a bacteriemia is proved, is that the prognosis is bad. I remember one case seen with Dr. Herrick; this patient recovered, but soon after died of another cause. A post-mortem showed a healed ulcer of the endocardium. That was the only patient I ever saw in my life who recovered from such a condition.

I believe that any drug treatment is absolutely useless. With regard to rheumatism, we do not know the cause, we have no specific medication to destroy the bacteria that might be the cause of the disease. We do not know, however, that the empirical employment of alkalies and salicylates does some good, and we have no specific treatment. Whether the endocarditis is due to the pneumococcus, the streptococcus, or the gonococcus, we have no agent that is specific. Consequently we must come to the serum or vaccine treatment. In two patients the antistreptococcus serum was used; one patient received two doses, the other repeated doses. But experience shows that if we are to use antistreptococcus serum successfully we must have a serum made from the strain of bacteria from which the patient suffers; the antistreptococcus serum in the market is practically useless unless it comes from the strain of bacteria of the same kind that affects the individual. Vaccination with pneumococcus or gonococcus has been absolutely negative so far as my experience goes. If given in too large doses, they do harm; in small doses they may modify the clinical course of the disease, reducing the temperature and pulse rate; this was the result in one patient; used in another patient it not only did no good, but did harm. In some cases leucocytosis was produced; the leucocytes, too, were rendered more phagocytic, but not bacteriolytic at all. Following the use of the normal serum in one case a chill occurred with high temperature, 104 or 105 F., thus substituting for the original fever a septic one. In some cases it seemed possible that there was a reduction in the number of colonies obtained from the individual's blood, as if the serum caused death of some bacteria in the circulating blood.

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PROCEEDINGS OF THE SESSION

TUESDAY, JUNE 8—AFTERNOON

The Section was called to order by the chairman, Dr. Joseph L. Miller, Chicago, at 2 p. m., at the Savoy Theater.

Dr. N. B. Potter, New York City, read a paper on "Medical Supervision of Boarding Schools, and Athletic Contests Among School Boys." Discussed by Drs. De Lancey Rochester, Buffalo; Richard C. Cabot, Boston; Stanley P. Black, Pasadena, Cal.; and N. B. Potter, New York.

Dr. Frederick Forchheimer, Cincinnati, read a paper on "Cardiac and Vascular Complications in Pneumonia, with Special Reference to Treatment." Discussed by Drs. De Lancey Rochester, Buffalo; Frank Billings, Chicago; C. F. Hoover, Cleveland; John H. Musser, Philadelphia; Alexander Lambert, New York City; Theodore Potter, Indianapolis, and F. Forchheimer, Cincinnati.

Dr. W. G. MacCallum, Baltimore, read a paper on "An Experimental Study of Gastric Tetany." Discussed by Drs. Allen A. Jones, Buffalo, and Nathaniel B. Potter, New York.

Dr. Frank Billings, Chicago, read a paper on "Chronic Infectious Endocarditis." Discussed by Drs. Alfred Stengel, Philadelphia; De Lancey Rochester, Buffalo; John A. Witherspoon, Nashville; Walter L. Bierring, Iowa City; John M. Anders, Philadelphia; Charles G. Stockton, Buffalo; Richard C. Cabot, Boston; and F. Billings, Chicago.

Dr. Allen A. Jones, Buffalo, read a paper on "Diverticulum of the Pylorus." Discussed by Drs. Charles G. Stockton, Buffalo; and A. A. Jones, Buffalo.

Dr. Warren Coleman, New York City, read a paper on "Diet in Typhoid Fever." Discussed by Drs. Max Einhorn, New York City; Frank E. Brown, Baltimore; Thomas A. Claytor, Washington; Arthur K. Stone, Boston; A. Jacobi, New York City; John M. Anders, Philadelphia; Walker, Philadelphia; Parker, Detroit; Woods Hutchinson, New York City, and W. Coleman, New York City.

WEDNESDAY, JUNE 9—MORNING

Dr. Judson Daland, Philadelphia, read a paper on "Clinical Significance of Indicanuria." Discussed by Drs. Heinrich Stern, New York City; Harry A. Harrower, Chicago; Richard

C. Cabot, Boston; Allen A. Jones, Buffalo;; Anthony Bassler, New York City; and J. Daland, Philadelphia.

Dr. Philip King Brown, San Francisco, read a paper on "The Diagnostic Value of Stained Specimens of Stools in Cancer of the Stomach." Discussed by Drs. Herman B. Allyn, Philadelphia; Allen A. Jones, Buffalo; Anthony Bassler, New York City; and P. K. Brown, San Francisco.

Dr. Alexander Lambert, New York City, read a paper on "Resorption of Proteids, Carbohydrates and Fats in the Chronic Alcoholic." Discussed by Drs. E. P. Joslin, Boston; John A. Lichty, Pittsburg; and A. Lambert, New York City.

Dr. Charles G. Stockton, Buffalo, read a paper on "The Diagnostic Value and Limitations of Analysis of the Gastric Contents."

Dr. A. W. Crane, Kalamazoo, Mich., read a paper on "*X*-Ray Evidence in Gastric Cancer."

Dr. Clifford B. Farr, Philadelphia, read a paper on "The Determination of Trypsin in the Stomach Contents After the Oil Test Meal."

These three papers were discussed by Drs. G. E. Pfahler, Philadelphia; Judson Daland, Philadelphia; Allen A. Jones, Buffalo; Richard C. Cabot, Boston; John A. Lichty, Pittsburg; Harry A. Harrower, Chicago; John N. Upshur, Richmond, Va.; C. W. Smith, Baltimore; Frank Smithies, Ann Arbor, Mich.; Alexander Lambert, New York City; Philip King Brown, San Francisco; C. G. Stockton, Buffalo; and A. W. Crane, Kalamazoo, Mich.

Dr. Charles P. Emerson, Clifton Springs, N. Y., read a paper on "The Diagnostic Importance of Examination of the Feces." Discussed by Drs. Henry F. Hewes, Boston; George Dock, New Orleans; David L. Edsall, Philadelphia; Woods Hutchinson, New York City, and Sir James Alexander Grant, Ottawa, Ontario.

Wednesday, June 9—Afternoon

Dr. James B. McElroy, Memphis, read the Oration in Medicine: "Tropical Diseases, America's Opportunities and Obligations."

The chairman appointed the following Nominating Committee: Drs. David L. Edsall, Philadelphia; D. Vanderhoof, Richmond, and Philip King Brown, San Francisco.

Dr. Samuel T. Darling, Ancon, Canal Zone, read a paper on "Transmission of Malarial Fever in the Canal Zone by Anopheles Mosquitoes." Discussed by Dr. Richard C. Cabot, Boston; John A. Witherspoon, Nashville; Seale Harris, Mobile, Ala., and S. T. Darling, Ancon, C. Z.

Dr. Simon Flexner, New York City, read a paper on "The Present Status of the Serum Treatment of Epidemic Cerebrospinal Meningitis." Discussed by Drs. Thomas Morgan Rotch, Boston; Philip King Brown, San Francisco; William Litterer, Nashville; and S. Flexner.

Dr. Herman N. Adler and Dr. Gerald Blake, Boston, presented a paper on "The Retention of Alkali by the Kidney, with Special Reference to Acidosis." Discussed by Dr. E. P. Joslin, Boston.

Dr. Sidney K. Simon, New Orleans, read a paper on "Amebic Dysentery." Discussed by Drs. T. B. Futcher, Baltimore; George Dock, New Orleans; Hobart A. Hare, Philadelphia; Hugo A. Freund, Detroit; James P. Tuttle, New York City; Samuel Goodman Gant, New York City; and S. K. Simon, New Orleans.

Thursday, June 10—Morning

Dr. Edward F. Wells, Chicago, secretary of the Committee on Program, stated that the conclusions reached by the committee were that the best interest of the Section on Medicine would be served by asking for a tentative recommendation of last year's report, and it asked that the matter be referred for further consideration to the Executive Committee, which should work out the problems involved. The report of the Committee on Program was as follows:

Your committee, in presenting this preliminary report, is of the opinion that a fair presentation of conclusions and recommendations of the subject of program methods which you have delegated to it would require much prolonged consideration that a full report should be presented to the Section at its session next year; meanwhile your indulgence and assistance are asked. At this time, however, the committee will make some suggestions which are thought useful to the Section officers for their consideration in preparing the program for the ensuing year. These are, broadly, as follows:

At the discretion of the Section officers there should be included in the program the following classes of papers:

A. A series of symposiums, each consisting of not more than three papers, the presentation of which shall be limited to not more than twenty minutes each, with discussions limited to not more than ten minutes for the first, and five minutes for each subsequent speaker.

B. A series of well-selected papers on highly important separate subjects, the presentation of which shall not exceed twenty minutes each, with discussion limited to ten minutes for the first and five minutes for each subsequent speaker.

C. A series of short papers, the presentation of each to be limited to ten minutes, with discussions limited to five minutes to each speaker.

D. A series of papers to be presented in full abstract, the reading of which shall not exceed five minutes, with discussion limited to five minutes for each speaker.

E. A series of highly scientific research papers, to be printed in full, and distributed to members on request, at least two weeks before the meeting, with written discussion, not exceeding four hundred words presented to the Secretary on the opening day's session, to which the author of the paper may have access, with an allowance of ten minutes for him to present his position and reply to the written criticisms filed.

The practical application of these suggestions is left to the untrammeled good judgment of the Section officers, offering the hearty cooperation of the committee, and requesting such cooperation on their part and on the part of the members of the Section, in the consideration of the entire problem, and in the formulating of conclusions for presentation at the next annual session.

In conclusion, it is the sense of the committee that while rules and regulations may aid in furnishing the work of the Section they cannot supplant the personal attention, judgment and discretion of the Section officers, but that on them in their preparation and management of the program and the conduct of the section work will largely depend the successful session.

In this connection it is recommended that fully accredited members make use of their prerogatives in rising to a point of order whenever time is trespassed on by members in the presentation of papers or in their discussions.

GEORGE DOCK, Chairman.
ALLEN JONES,
ALEXANDER LAMBERT.
EDWARD F. WELLS, Secretary.

Dr. DeLancey Rochester, Buffalo, moved that the report be received and that the recommendations be adopted. The motion was seconded and carried.

The Nominating Committee made the following report: Chairman, Dr. George Blumer, New Haven; secretary, Dr. Wilder Tileston, Boston; orator, Dr. Richard C. Cabot, Boston; delegate, Dr. Joseph Capps, Chicago; alternate delegate, Dr. Alexander Lambert, New York City.

Dr. Munson moved the adoption of the report; the motion was carried.

Dr. Warfield T. Longcope, Philadelphia, read a paper on "The Association of Aortic Insufficiency with Syphilitic Aortitis." Discussed by Drs. Richard C. Cabot, Boston; Allen A. Jones, Buffalo; and W. T. Longcope, Philadelphia.

Dr. Henry A. Christian, Boston, read a paper on "Clinical Value of Recent Studies in Experimental Nephritis."

Dr. John H. Musser, Philadelphia, read a paper on "Hypertension in Nephritis; Its Cause and Treatment."

Dr. Victor C. Vaughan, Ann Arbor, being unable to attend, by a vote of the Section his paper on "The Value and Limitations of a Salt-Free Diet and Restriction of Fluids in Nephritis," was read for him by Dr. H. W. Hewlett, Ann Arbor.

Dr. Edward F. Wells, Chicago, read a paper on "The Management of Uremia."

These four papers were discussed by Drs. David L. Edsall, Philadelphia; Albert Robin, Wilmington, Del.; De Lancey Rochester, Buffalo; James Tyson, Philadelphia; John A. Lichty, Pittsburg; John N. Upshur, Richmond, Va..; C. W. Smith, Baltimore; Walter L. Bierring, Iowa City, Iowa; Heinrich Stern, New York City; Boardman Reed, Los Angeles; Hugo A. Freund, Detroit; C. F. Hoover, Cleveland; H. A. Christian, Boston; J. H. Musser, Philadelphia; and E. F. Wells, Chicago.

Dr. George Dock, New Orleans, read a paper on "The Talma-Morrison Operation in the Treatment of Cirrhosis of Liver." Discussed by Drs. Nathaniel Bowditch Potter, New York City; Albert E. Roussel, Philadelphia; C. F. Hoover, Cleveland; S. E. Munson, Springfield, Ill.; Joseph L. Miller, Chicago; and G. Dock, New Orleans.

Thursday, June 10—Afternoon

Dr. McCrea read the report of Committee on Revision of Pharmacopeia (See page 320). Discussed by Drs. M. I. Wilbert, Philadelphia; L. A. Conner, New York City; John F. Anderson, Washington, D. C.; W. Clayton Thrush, Philadelphia.

Dr. H. T. Ricketts, Chicago, read a paper on "Rocky Mountain Spotted Fever." Discussed by Dr. Woods Hutchinson, New York City.

Dr. Thomas D. Coleman, Augusta, Ga., read a paper on "Algid Forms of Malaria, with Report of Cases." Discussed by Drs. John A. Witherspoon, Nashville; James B. McElroy, Memphis; and T. D. Coleman, Augusta, Ga.

Dr. Edward H. Goodman, Philadelphia, read a paper on "The Value of Alimentary Levulosuria in the Diagnosis of

Hepatic Cirrhosis." Discussed by Drs. De Lancey Rochester, Buffalo; Williams, Rochester; and E. H. Goodman, Philadelphia.

Dr. S. P. Beebe and Dr. W. Gilman Thompson, New York City, read a paper on "The Nature and Treatment of Anemia." Discussed by Drs. De Lancey Rochester, Buffalo; Theodore Potter, Indianapolis; Louis G. Heyn, Cincinnati; Samuel L. Miller, Chicago; Walter L. Bierring, Iowa City, Iowa; and S. P. Beebe, New York City.

Dr. Joseph H. Pratt, Boston, read a paper on "The Work of a Cooperative Hydrotherapeutic Establishment." Discussed by Drs. John A. Lichty, Pittsburg; C. W. Smith, Baltimore; Andrew MacFarlane, Albany, N. Y.; and J. H. Pratt, Boston.

REPORT OF THE COMMITTEE ON THE PHARMACOPEIA

It has not been the aim of this committee to do more than bring forward what seemed to be the changes which might advisedly be made in the revision of the Pharmacopeia from the standpoint of the clinician. There are many points which the general committee on the revision have to consider which do not specially concern us. As is well known there are many interests to be considered, perhaps how many only those on the committee have any idea. The discussions of these, however, is not in place here, and it seems advisable to take up only those points which may profitably be considered by the clinician.

What should the Pharmacopeia include? Should it be kept to the smallest limits or allowed to expand? Should every drug which is included in it be carefully scanned at intervals to see if its position is still deserved? Should additions be looked at with careful scrutiny or should we go on the principle that everything which the profession uses should be included? Should combinations of drugs be admitted or not? Should proprietary or patented remedies be admitted to it? Should Tct. X Co. be in the Pharmacopeia when Tct. Y Co. is not? Ask yourself some of these questions put them to your friends and you begin to realize how many views there are. It is probably not our province to pass on these, but still we may say something.

Under the title, "The Capture of the Pharmacopeia; With Suggestions for its Recapture," Leffman[1] has pointed out what a small proportion of the committee on the last revision was composed of clinicians, the majority being pharmacists. A reversal of these numbers would seem to be in order—yet it can safely be said that the majority of the profession take little interest in the Pharmacopeia, know little about it, and do not feel that it really concerns them. This is a matter which we should regard very seriously and anything which can aid in making the Pharmacopeia more used as a handbook by the profession is well worthy of consideration. Of course there are many causes for this and the remedy lies in various lines, such as the proper instruction of students in their at-

1. Read before the Philadelphia County Medical Society, March 24, 1909.

titude towards and knowledge of it. But these hardly come in the province of this discussion.

It will be granted that it would be a great advantage to have the profession more familiar with it and as far as possible using the drugs therein contained. That there are certain drugs which will be used and cannot be admitted is evident. For one thing the revision takes place only at intervals and new substances protected by a trademark or patent must be considered. At present many of them are in extensive use. But the great bulk of the drugs which we need to use are found in it. Probably a certain number of the profession will use substances or combinations which can never be admitted. The more they know about the Pharmacopeia the fewer will belong to this class. To have the Pharmacopeia used more extensively by the profession seems an important matter and the more convenient it can be made, the more closely we can bring the drugs in it to correspond with the ones in active use, the better.

An important point which should be kept in mind is the possibility of making the Pharmacopeia something which will come into constant use by the members of the profession generally. In bringing this about one important thing is the reduction in size, which seems to be a point worth considering. Might it not be possible to omit the appendix? The reply may be made that this is an integral part of what the Pharmacopeia should be and yet for the medical profession it is of little importance. Perhaps an edition for the profession might be published in which the various directions regarding preparations, which belong more strictly to the pharmacy side, might be omitted. Another point which is put forward for discussion is in regard to the publication of an annual bulletin, such as has been brought out by the American Medical Association. The value of this to the profession has been tremendous and we owe a great many thanks to those who have done the work of its preparation. Would it be possible to have a somewhat smaller publication in association with the Pharmacopeia brought out every year or every second year? If this were done the profession would probably regard the Pharmacopeia more as a volume dealing with everyday things than as a record of the past. It may be the general opinion that this is better left to the American Medical Association, but the advisability of the other course seems worthy of consideration. This would not exclude the work at present being done and might be carried on in conjunction with it.

Another point is as to the advisability of introducing any substance "which cannot be produced otherwise than under a

patented process or which is protected by proprietary rights." The advisability of doing this is hinted at in the eighth Pharmacopeia. Your committee feels that this would be a mistake and that the position taken in the last Pharmacopeia should be maintained. To do otherwise is to admit the thin edge of what would prove to be a very large wedge. Certain drugs might be omitted without any harm being done but who is to draw the line? It seems safer to hold by the present rule; there is less danger in that than in the other case. How many of the preparations which would have been admitted ten years ago, would be considered worthy of a place to-day? How many which might be regarded as worthy of a place to-day would be retained ten years from now? At the same time one must recognize that there is much to be said for the other view, that under proper safeguards some of them might be admitted.

Drugs which should be dropped from the Pharmacopeia. It may be thought well to retain some of these in the National Formulary for various reasons. The majority do not seem to deserve a place and should be dropped for want of sufficient recognition and use. Some are used in certain localities, but this should not justify their retention.

Acetum Opii.
Acidum Camphoricum
Aconitina: (This should be dropped on account of its strength and variability as well as the dangers of poisoning.)
Adeps: (The use of this has almost entirely ceased. It has been replaced by more suitable substances.)
Althea.
Anthemis.
Berberis: Fluidextractum Berberidis.
Calamus: Fluidextractum Calami.
Calendula: Tinctura Calendulæ.
Cassia Fistula.
Chimaphila: Fluidextractum Chimaphilæ.
Chirata: Fluidextractum Chiratæ.
Cimicifuga: (Tincturæ Cimicifugæ; Fluidextractum Cimicifugæ; Extractum Cimicifugæ.)
Cinchonidinæ.
Cinchoninæ Sulphas.
Cypripedium: Fluidextractum Cypripedii.
Euonymus: (Fluidextractum Euonymi; Extractum Euonymi.)
Eupatorium: Fluidextractum Eupatorii.
Frangula: Fluidextractum Frangulæ.
Gambir: (Tinctura Gambir Composita; Trochisci Gambir.)
Geranium: Fluidextractum Geranii.
Hedeoma: Oleum Hedeomæ.
Krameria: (Tinctura Krameriæ; Fluidextractum Krameriæ; Extractum Krameriæ; Syrupus Krameriæ; Trochisci Krameriæ.)
Lappa: Fluidextractum Lappæ.
Linimentum Saponis Mollis: (This causes confusion as it is not intended to be used as an embrocation. The same might be changed.)

Marrubium.
Matico: Fluidextractum Matico.
Matricaria.
Mezereum: Fluidextractum Mezerei.
Oleum Coriandri.
Oleum Erigerontis.
Oleum Sabinæ.
Oleum Sinapis Volatile.
Pareira: Fluidextractum Pareiræ.
Phytolacca: Fluidextractum Phytolaccæ.
Pimenta: Oleum Pimentæ.
Piperina.
Pulvis Acetanilidi Compositus: (There does not seem any reason for retaining this combination.)
Quillaja: (Fluidextractum Quillajæ; Tinctura Quillajæ)
Rhus Glabra: Fluidextractum Rhois Glabræ.
Rubus: (Fluidextractum Rubi; Syrupus Rubi.)
Sabal: Fluidextractum Sabal.
Safrolum.
Salvia.
Scutellaria: Fluidextractum Scutellariæ.
Staphisagria: Fluidextractum Staphisagriæ.
Stillingia: Fluidextractum Stillingiæ.
Unguentum Potassii Iodidi.
Unguentum Zinci Stearatis.
Unguentum Hydrargyri and Unguentum Hydrargyri Dilutum: (Much confusion is caused by these two ointments and one should be dropped.)
Xanthoxylum: Fluidextractum Xanthoxyli.

In regard to the question of additions, the committee recommends that the physiologic standard for the strength of certain drugs be adopted. Among these we should suggest digitalis, strophanthus and ergot. At present various methods are used, and it would seem wise that a definite standard should be laid down. Regarding the drugs which should be added, the following seem worthy of consideration:

Calcium Lactate: This is being used more and more and is rapidly replacing calcium chlorid.

Phenolphthalein: This has come quite extensively into use and its value seems to be definitely established. It might possibly be wise to add the preparation which can be given hypodermically.

Arsenic: The use of arsenic has increased a great deal of late, especially its hypodermic administration, and it seems wise to have some preparations in the Pharmacopeia which can be readily used in this way. Of these the value of sodium cacodylate and sodium aminophenyl arsenate seems definitely established.

Theobromin: The value of this seems sufficiently established.

Bile Salts: The suggestion that their inclusion be considered seems worthy of consideration.

Diacetyl-morphin and *Theobromin-sodio-salicylate* are extensively used and worthy of being added.

It may seem that the number of drugs to be included is in striking disproportion to the number struck out. The overgrown condition of the Pharmacopeia supports the advisability of this. There seems good ground for the feeling that we should go slowly in adding to what has too much already.

JOSEPH A. CAPPS, Chicago.
JOSEPH H. PRATT, Boston.
THOMAS MCCRAE, Baltimore.
JOHN T. HALSEY, New Orleans.

ABSTRACT OF DISCUSSION

MR. M. I. WILBERT, Washington, D. C.: From a pharmaceutical point of view the report is a very pleasing one. There can be no doubt but that members of the medical profession should absolutely dictate the contents of the Pharmacopeia. That is their province, it is their duty. The Committee on Revision of the Pharmacopeia is often mistaken for the revision convention. We frequently hear that the clinician, the medical practitioner, is not represented on the revision committee; as a matter of fact the clinician requires no representation on the revision committee at all. There is nothing in connection with the work of the revision committee that is of any direct interest to him, or to which he can contribute materially; he would hamper rather than aid the work of revision. The medical profession should dictate what the Pharmacopeia should contain and the method of providing it.

Much has been said about the size of the Pharmacopeia. Here again the medical man should insist that a more distinct division be made between pharmacopeial matters proper and the chemical tests. Much of the material now in the Pharmacopeia itself could be relegated to this appendix, and thus divide the Pharmacopeia into two volumes; one the Pharmacopeia proper which the physician could use and which would contain all the information he wanted, while the combined volumes should contain all the information the pharmacist needs and must have. As the report states, the function of the Pharmacopeia is primarily one of standards; it should be simply one of standards and not a medical lexicon. If the standards are correct they do not need changing annually and only such changes need be made as are found necessary to correct palpable errors. The more or less ephemeral drugs are sufficiently well defined by the Council on Pharmacy and Chemistry of the American Medical Association in "New and Nonofficial Remedies."

Ninety years ago, when the United States Pharmacopeia was originated, it was in the hands of medical practitioners who had a wide scope of vision. They wished to make the book valuable and to keep it in harmony with the standards established abroad. Singularly enough, that idea prevailed

until the Pharmacopeia came to be revised by pharmacists and converted into a book on pharmacy. In 1902, an international congress was held in Brussels for the purpose of establishing standards for potent medicaments. Among the articles acted on was mercurial ointment; a 33 per cent. ointment of mercury was adopted as an international standard. The Committee on Revision of the United States Pharmacopeia, in attempting to comply with the international requirements, introduced a diluted mercurial ointment, or blue ointment, which, by the way, is not blue at all, but green, and does not comply with international standards except so far as its strength is concerned. If the Pharmacopeia is to meet the needs of the medical profession true international standards must be insisted on.

I wish to congratulate the profession on the tone of the report. If the medical practitioners of the country will assume a more dictatorial policy, the next Pharmacopeia of the United States will be of value to the medical man and a real necessity to the pharmacist.

Dr. Lewis A. Conner, New York: The difficulties attending the selection of the more or less obsolete drugs to be dropped from, and the new drugs to be added to, the Pharmacopeia are many and great. The recommendation of the committee as to the drugs to be dropped will, I think, be generally approved. They can all well be spared. The number of drugs recommended for admission, however, is, it seems to me, regrettably small, and the reason for this lies in the fact that the committee has decided not to recommend any drug which has been patented. However much we may prefer to use unpatented drugs, the fact remains that practically all the modern, synthetic drugs are so patented, and among this number are many remedies in constant, daily use, which could not be dispensed with without the serious crippling of our therapeutic resources. Such drugs, for example, as aspirin, adrenalin, argyrol, heroin, ichthyol, veronal—to mention only a few out of many—shall we abandon their use merely because they are patented? I think few would venture to recommend so radical a course. But, if we are to continue to use them, should they not, if they have proved their usefulness, have a place in the Pharmacopeia? It seems to me that they should.

It will be generally admitted, I think, that the Pharmacopeia at present fails to meet the needs of the practicing physician and has lost its position as guide and book of reference in his daily work. The reason for this is chiefly that in it he seeks in vain for information concerning many of the drugs is general use. It is idle to expect that he will abandon the use of drugs merely because they are not to be found in the Pharmacopeia. It is much more likely that he will discard the Pharmacopeia itself. One of the very best evidences that the Pharmacopeia does not at present meet the require-

ments of physicians is the fact that this Association has felt it necessary to publish the two admirable little volumes, "Physicians' Manual of the Pharmacopeia and National Formulary" and "New and Nonofficial Remedies."

If the Pharmacopeia is to regain its position of prestige and usefulness, so far as it concerns physicians, some radical changes in its policy are necessary. In my judgment, the most important of these are: First, the publication of a greatly abridged "Physicians' Edition," as has been suggested by Mr. Wilbert. Second, the inclusion of the more trustworthy and useful of the modern, synthetic drugs, whether they be patented or not. Third, the issuance at frequent (perhaps yearly) intervals of bulletins recording the changes which have been made, the new drugs introduced, the undesirable ones dropped. With the enormous yearly output of new drugs, a certain small proportion of which are really valuable, it is idle to suppose that a volume of this sort which is revised only once in a decade can keep abreast of current practice. The needed flexibility can be obtained, I think, only by the publication of such bulletins at comparatively short intervals.

DR. JOHN F. ANDERSON, Washington, D. C.: One very important agent has been omitted from the list of proposed additions to the Pharmacopeia, namely, tetanus antitoxin. Diphtheria antitoxin was admitted to the Eighth Decennial Revision of the Pharmacopeia following the promulgation of a standard unit for diphtheria antitoxin by the U. S. Public Health and Marine-Hospital Service. On Oct. 25, 1907, a standard American unit for measuring the strength of tetanus antitoxin was promulgated by the same laboratory. The great value of tetanus antitoxin as a prophylactic alone certainly entitles it to admission to the Pharmacopeia, and I hope that it will be included in the next revision.

DR. M. CLAYTON THRUSH, Philadelphia: A smaller edition of the Pharmacopeia for the use of clinicians should include the Latin and English name of each drug, its synonym, a description of the important characteristics of the drug, its dose, solubility and compatibility, with therapeutic action expressed in a few words, and a few other particulars; which is all the average clinician wishes. Such a book could be bought for about fifty cents. A book entitled the "Physicians' Manual of the Pharmacopeia and National Formulary," published by the American Medical Association, contains those very facts; it is a small book and gives the official name, synonyms, characteristics, doses, therapeutic indications, etc. This is really all the physician needs. Therefore, why not supply ourselves with such a manual; in it could be inserted year by year the drugs that the Council on Pharmacy and Chemistry has examined and recommended.

With regard to the admission of new drugs, there is one drug that is largely used at the present time and under so

many different names, viz., the active principle of the adrenal gland. This is supplied under different names by the different manufacturers, but all preparations are of the same strength, 1 to 1,000 in normal salt solution. Why not make this official? At present the gland itself only is official. But only about one physician in one thousand uses the gland; all others always use the active principle.

Hallberg collected one million prescriptions in order to show what drugs were most used in this country. He found that saw palmetto, while only prescribed about three time in a thousand prescriptions in Philadelphia, was prescribed over thirty times in Chicago, and so it is with all those drugs if we but investigate. There are drugs used in one portion of the country that are not at all used in another portion. A Pharmacopeia should not be one designed for Philadelphia alone, but for the United States. Therefore, it is important that all the drugs in use all over the country should be included. Here is another point that should be borne in mind; while these drugs are practically of no use, I believe they should be placed in a special place and not entirely dropped, for they may be of some service to certain practitioners in certain localities.

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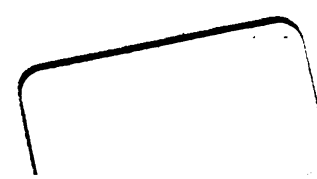

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